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THEARLUST ENTERED AT 14:46:35 ON 31 JUL 2002)
                                                                        - Key terms
            602 SEA FILE=HCAPLUS ABB=ON PLU-ON-(+STREPTOCOCC? OR
L10
                S) (W) PNEUMON?) (5A) INFECTION
            176 SEA FILE=HCAPLUS ABB=ON PLU=ON L10(S) (TREAT? OR
L15
                THERAP? OR PROPHYL?)
             25 SEA FILE=HCAPLUS ABB=ON PLU=ON L15(S) (PROTEIN OR
L16
                POLYPROTEIN OR PEPTIDE OR POLYPEPTIDE)
L16 ANSWER 1 OF 25
                     HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER:
                         2002:522026 HCAPLUS
                         Use of surface-associated pneumo protective
TITLE:
                         protein of Streptococcus
                         pneumoniae in diagnosis and
                         treatment of infection and
                         inflammation
                         Green, Bruce A.; Masi, Amy W.
INVENTOR(S):
                         Wyeth, John, and Brother Ltd., USA
PATENT ASSIGNEE(S):
                         PCT Int. Appl., 91 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
                         English
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                                           APPLICATION NO.
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     PATENT NO.
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1860

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2002053761 A2 20020711 WO 2001-US49650 20011228

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2000-258841P P 20001228

The present invention discloses amino acid sequences and nucleic acid sequences relating to a Streptococcus Pneumoniae surface assocd. Pneumo Protective Protein 1 (PPP1) having a mol. wt. of about 20 kilo Daltons (kDa), an isoelec. point of 4.587 and a charge of -14.214 at pH 7.0. The PPP1 exhibits the ability to reduce colonization of pneumococcal bacteria. Thus the present invention also pertains to compns. for the treatment and prophylaxis of infection or inflammation assocd. with bacterial infection.

L16 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2002:359275 HCAPLUS

TITLE:

Nucleic acids and proteins from group B Streptococcus agalactiae and group  ${\bf A}$ 

Streptococcus pyogenes

INVENTOR(S):

Telford, John; Masignani, Vega; Margarit Y Ros,

Immaculada; Grandi, Guido; Fraser, Claire;

Tettelin, Herve

PATENT ASSIGNEE(S):

Chiron S.P.A., Italy; The Institute for Genomic

Research

Searcher :

Shears

308-4994

SOURCE:

PCT Int. Appl., 4525 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
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       WO 2002034771
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                                                               WO 2001-XB4789
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PRIORITY APPLN. INFO.:
                                                           GB 2000-26333
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                                                           GB 2000-28727
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                                                           WO 2001-GB4789
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                                                                                        20011029
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AB The invention provides proteins from group B streptococcus (Streptococcus agalactiae) and group A streptococcus (Streptococcus pyogenes), including amino acid sequences and the corresponding nucleotide sequences. The nucleotide sequence of the full genome of S. agalactiae strain 2603 V/R is provided as are 5483 protein-coding genes and the amino acid sequences of their protein products. Data are given to show that the proteins are useful antigens for vaccines, immunogenic compns., and/or diagnostics. The proteins are also targets for antibiotics to treat or prevent bacterial infection, and in particular, streptococcal infection. [This abstr. record is one of three records for this document necessitated by the large no. of index entries required to fully index the document and publication constraints.].

L16 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2002:359274 HCAPLUS

TITLE:

Nucleic acids and proteins from group B

Streptococcus agalactiae and group A

Streptococcus pyogenes

INVENTOR(S):

Telford, John; Masignani, Vega; Margarit Y Ros,

Immaculada; Grandi, Guido; Fraser, Claire;

Tettelin, Herve

Chiron S.P.A., Italy; The Institute for Genomic PATENT ASSIGNEE(S):

Research

PCT Int. Appl., 4525 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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               TD, TG
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     WO 2002034771
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                                              GB 2000-26333
                                                                 A 20001027
PRIORITY APPLN. INFO.:
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                                                                 A 20001124
                                              GB 2001-5640
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                                              WO 2001-GB4789
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The invention provides proteins from group B streptococcus AΒ (Streptococcus agalactiae) and group A streptococcus (Streptococcus pyogenes), including amino acid sequences and the corresponding nucleotide sequences. The nucleotide sequence of the full genome of S. agalactiae strain 2603 V/R is provided as are 5483 protein-coding genes and the amino acid sequences of their protein products. Data are given to show that the proteins are useful antigens for vaccines, immunogenic compns., and/or diagnostics. The proteins are also targets for antibiotics to treat or prevent bacterial infection, and in particular, streptococcal infection. [This abstr. record is one of three records for this document necessitated by the large no. of index entries required to fully index the document and publication constraints.].

L16 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2002:332211 HCAPLUS

DOCUMENT NUMBER:

136:364951

TITLE:

Nucleic acids and proteins from group B

Shears 308-4994 Searcher :

Streptococcus agalactiae and group A

Streptococcus pyogenes

INVENTOR(S):

Telford, John; Masignani, Vega; Margarit y Ros,

Immaculada; Grandi, Guido; Fraser, Claire;

Tettelin, Herve

PATENT ASSIGNEE(S):

Chiron S.P.A., Italy; The Institute for Genomic

Research

SOURCE:

PCT Int. Appl., 4525 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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APPLICATION NO.
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                 TD, TG
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                                                          WO 2001-XB4789
      WO 2002034771
                                    20020502
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                 TD, TG
                                                       GB 2000-26333
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PRIORITY APPLN. INFO.:
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                                                       GB 2000-28727
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                                                       WO 2001-GB4789
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The invention provides proteins from group B streptococcus AB (Streptococcus agalactiae) and group A streptococcus (Streptococcus

pyogenes), including amino acid sequences and the corresponding nucleotide sequences. The nucleotide sequence of the full genome of S. agalactiae strain 2603 V/R is provided as are 5483 protein-coding genes and the amino acid sequences of their protein products. Data are given to show that the proteins are useful antigens for vaccines, immunogenic compns., and/or diagnostics. The proteins are also targets for antibiotics to treat or prevent bacterial infection, and in particular, streptococcal infection. [This abstr. record is one of three records for this document necessitated by the large no. of index entries required to fully index the document and publication constraints.].

L16 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2002 ACS 2002:293824 HCAPLUS

ACCESSION NUMBER: DOCUMENT NUMBER:

136:321986

TITLE:

Drug screening for effectors of enoyl ACP reductase encoded by fabK and fabI genes of Streptococcus pneumoniae for treatment of

bacterial infections

INVENTOR(S):

Dewolf, Walter E., Jr.; Payne, David J.; Seefeld, Mark A.; Wallis, Nicola G.; West, Joshua M.; Brandt, Martin; Keller, Paul M.; Patel, Arunbhai H.; Reed, Shannon L.; Tew, David

G.

KIND

PATENT ASSIGNEE(S):

Smithkline Beecham Corporation, USA; Smithkline

ADDITONTON NO

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Beecham P.L.C.

SOURCE:

PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent LANGUAGE:

English

DAME

FAMILY ACC. NUM. COUNT: 1 .

PATENT INFORMATION: DAMENIO NO

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		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KΡ,	KR,	LC,	LK,	LR,	LT,	LV,
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WO 2002031128 A1 20020 W: AE, AL, AU, BA, BB, GM, HR, HU, ID, IL, MA, MG, MK, MN, MX, TT, TZ, UA, US, UZ, TJ, TM RW: GH, GM, KE, LS, MW, CY, DE, DK, ES, FI, BF, BJ, CF, CG, CI, The invention provides method Fabk gene encoded enoyl ACP metab. of bacteria or to tre screening of inhibitors of E reductase) are also provided and amino acid sequences of provided.	WO 2002031128 Al 20020418 W: AE, AL, AU, BA, BB, BG, GM, HR, HU, ID, IL, IN, MA, MG, MK, MN, MX, MZ, TT, TZ, UA, US, UZ, VN, TJ, TM RW: GH, GM, KE, LS, MW, MZ, CY, DE, DK, ES, FI, FR, BF, BJ, CF, CG, CI, CM, The invention provides methods to FabK gene encoded enoyl ACP redumetab. of bacteria or to treat to screening of inhibitors of FabI reductase) are also provided. It and amino acid sequences of the provided.	WO 2002031128 A1 20020418  W: AE, AL, AU, BA, BB, BG, BR, GM, HR, HU, ID, IL, IN, IS, MA, MG, MK, MN, MX, MZ, NO, TT, TZ, UA, US, UZ, VN, YU, TJ, TM  RW: GH, GM, KE, LS, MW, MZ, SD, CY, DE, DK, ES, FI, FR, GB, BF, BJ, CF, CG, CI, CM, GA, The invention provides methods for use and amino acid sequences of the encoprovided.	WO 2002031128 A1 20020418 WC W: AE, AL, AU, BA, BB, BG, BR, BZ, GM, HR, HU, ID, IL, IN, IS, JP, MA, MG, MK, MN, MX, MZ, NO, NZ, TT, TZ, UA, US, UZ, VN, YU, ZA, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, CY, DE, DK, ES, FI, FR, GB, GR, BF, BJ, CF, CG, CI, CM, GA, GN, The invention provides methods for using FabK gene encoded enoyl ACP reductase, presented of bacteria or to treat bacterial screening of inhibitors of FabI gene (correductase) are also provided. Nucleic and amino acid sequences of the encoded provided.	WO 2002031128 Al 20020418 WO 200 W: AE, AL, AU, BA, BB, BG, BR, BZ, CA, GM, HR, HU, ID, IL, IN, IS, JP, KP, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, CY, DE, DK, ES, FI, FR, GB, GR, IE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, The invention provides methods for using ago FabK gene encoded enoyl ACP reductase, partimetab. of bacteria or to treat bacterial into screening of inhibitors of FabI gene (coding reductase) are also provided. Nucleic acid and amino acid sequences of the encoded enoy provided.	WO 2002031128 A1 20020418 WO 2000-US W: AE, AL, AU, BA, BB, BG, BR, BZ, CA, CN, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, The invention provides methods for using agonist FabK gene encoded enoyl ACP reductase, particula metab. of bacteria or to treat bacterial infecti screening of inhibitors of FabI gene (coding for reductase) are also provided. Nucleic acid sequand amino acid sequences of the encoded enoyl ACP provided.	WO 2002031128 A1 20020418 WO 2000-US2762 W: AE, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CZ, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, The invention provides methods for using agonists ar FabK gene encoded enoyl ACP reductase, particularly metab. of bacteria or to treat bacterial infection. screening of inhibitors of FabI gene (coding for encreductase) are also provided. Nucleic acid sequence and amino acid sequences of the encoded enoyl ACP reductase.	WO 2002031128 A1 20020418 WO 2000-US27628 20 W: AE, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CZ, DZ, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, TJ, TM  RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, The invention provides methods for using agonists and an FabK gene encoded enoyl ACP reductase, particularly to metab. of bacteria or to treat bacterial infection. Metascreening of inhibitors of FabI gene (coding for enoyl Aceptal coding agonists and amino acid sequences of the encoded enoyl ACP reductase) are also provided. Nucleic acid sequences of and amino acid sequences of the encoded enoyl ACP reductation.	WO 2002031128 A1 20020418 WO 2000-US27628 20001 W: AE, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CZ, DZ, EE, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, The invention provides methods for using agonists and antagorabk gene encoded enoyl ACP reductase, particularly to modul metab. of bacteria or to treat bacterial infection. Methods screening of inhibitors of FabI gene (coding for enoyl ACP reductase) are also provided. Nucleic acid sequences of ger and amino acid sequences of the encoded enoyl ACP reductase provided.	WO 2002031128 A1 20020418 WO 2000-US27628 20001006 W: AE, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CZ, DZ, EE, GE, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, The invention provides methods for using agonists and antagonist FabK gene encoded enoyl ACP reductase, particularly to modulate metab. of bacteria or to treat bacterial infection. Methods for screening of inhibitors of FabI gene (coding for enoyl ACP reductase) are also provided. Nucleic acid sequences of gene fa and amino acid sequences of the encoded enoyl ACP reductase are provided.

THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

HCAPLUS COPYRIGHT 2002 ACS L16 ANSWER 6 OF 25

ACCESSION NUMBER:

2002:275751 HCAPLUS

DOCUMENT NUMBER:

136:290805

308-4994 Searcher : Shears

TITLE: Mucin binding proteins and their variants from

Streptococcus pneumoniae and their use in

diagnosis and treatment of infections

Green, Bruce A.; Masi, Amy W.; Reddy, Molakala INVENTOR(S):

PATENT ASSIGNEE(S): American Home Products Corporation, USA; The

Research Foundation of S.U.N.Y.

PCT Int. Appl., 71 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	CENT 1	NO.		KI	ND	DATE			A	PPLI	CATI	и ис	٥. ِ	DATE		
									_							
WO	2002	0283	51	A	2	2002	0411		W	0 20	01-U	S312	69	2001	1004	
	W:	AE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,
		GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LC,
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NO,
		ΝZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,
		TZ,	UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,
		,	ТJ,													
	RW:					MW,										
		CY,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,
		TR,	BF,	ΒJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,
		TD,	TG													
PRIORITY	APP	LN.	INFO	. :								88P	_	2000		
									US 2	001-	2671	04P	Ρ	2001	0207	

The present invention provides for amino acid and nucleic acid AΒ sequences of isolated mucin-binding proteins (MBP) from Streptococcus pneumoniae and fragments thereof. More specifically, mucin-binding proteins of 12 kDa and 14 kDa were identified using a 10-20% SDS-PAGE gel. Expression vectors, transfected host cells, methods for producing recombinant mucin-binding proteins, compns. comprising the proteins, and antibodies to the proteins also are contemplated. A method of inducing an immune response is described by the present invention. Screening and diagnosing methods are provided for otitis media, bacteremia pneumonia, meningitis, rhino sinusitis and lower respiratory tract infections using MBP of the present invention. In a specific embodiment, lysine variants of MBP are provided wherein the absence of at least one lysine residue decreases mucin-binding protein activity. Mucosal immunization with 12 kDa MBP was shown to reduce pneumococcal colonization in the mouse nasopharynx.

HCAPLUS COPYRIGHT 2002 ACS L16 ANSWER 7 OF 25

ACCESSION NUMBER: DOCUMENT NUMBER:

2002:242363 HCAPLUS

136:305830

TITLE:

Streptococcus pneumoniae ffh gene and protein sequences and characterization of Staphylococcus aureus ffh ribonucleoprotein binding to 4.5S RNA

for use in high-throughput drug screening Cheever, Christy; Fecteau, Douglas; Li, Hu;

INVENTOR(S):

PATENT ASSIGNEE(S):

Payne, David; Steel, Angela; Wang, Lei Smithkline Beecham Corp, USA; Smithkline Beecham

P.L.C.

Brit. UK Pat. Appl., 55 pp. SOURCE:

CODEN: BAXXDU

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

KIND DATE APPLICATION NO. PATENT NO. \_\_\_\_\_\_ 20020116 GB 2001-7127 20010321 GB 2364053 A1 US 2000-191008P P 20000321 PRIORITY APPLN. INFO.: The present invention provides the protein and nucleotide sequences of ffh (fifty four homolog) of Streptococcus pneumoniae. The invention also provides the initial ribonucleoprotein interaction of the ffh protein of Staphylococcus aureus and the 4.5S RNA. This may be used for high-throughput drug screening for effectors of this interaction. This invention may be used for treating otitis media, conjunctivitis, pneumonia, bacteremia, meningitis, sinusitis, pleural emphysema and endocarditis and most particularly meningitis caused by Streptococcus pneumoniae or Staphyloccus aureus. Dissocn. const. (Kd) for interaction of N-His-tagged ffh protein of S. aureus and 4.5S RNA was 110 nM. Dissocn. const. (Kd) for interaction of S. aureus and Esherichia coli ffh proteins with S. aureus TAMRA-labeled 28-mer 4.5S RNA oligomer, demonstrated by fluorescence polarization binding assays were 200 nM and 580 nM, resp. Specificity of the binding interaction between TAMRA-labeled 28-mer 4.5S RNA oligomers and ffh protein of S. aureus was also demonstrated.

L16 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2001:798256 HCAPLUS

DOCUMENT NUMBER:

135:343285

TITLE:

Immunogenic pneumococcal protein and vaccine

compositions thereof

INVENTOR(S):

Koenig, Scott; Johnson, Leslie S.; Amadou, John

PATENT ASSIGNEE(S):

SOURCE:

Medimmune, Inc., USA PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATEN	I TV	10.		KI	ND I	DATE			A	PPLI	CATI	и ис	ο.	DATE		
WO 20	0010	813	30	A	2	2001	1101		W	200	01-U	S138:	28	2001	0427	
WO 20	0010	813	80	Α	3 :	2002	0228									
V	₹:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GΕ,
		GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NO,
		NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	·TR,	TT,
		TZ,	UA,	UG,	UZ,	VN,	YU,	ZA,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,
		ТJ,	TM													
F	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ŻW,	ΑT,	BE,	CH,
		CY,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	·LU,	MC,	NL,	PT,	SE,
										-	-			NE,		

US 2000-200074P P 20000427 PRIORITY APPLN. INFO.: The present invention relates to novel immunogenic polypeptides, and therapeutically active fragments thereof, and vaccines, and vaccine compns., for the prevention and treatment of streptococcal infection, esp. by Streptococcus pneumoniae. The invention also relates to antibodies against the disclosed polypeptides, as well as methods of disease prevention and/or treatment. L16 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2002 ACS 2001:114787 HCAPLUS ACCESSION NUMBER: DOCUMENT NUMBER: 134:177340 Pneumococcal vaccines TITLE: De Groot, Ronald; Hermans, Peter Wilhelmus Maria INVENTOR(S): Erasmus Universiteit Rotterdam, Neth. PATENT ASSIGNEE(S): Eur. Pat. Appl., 18 pp. SOURCE: CODEN: EPXXDW DOCUMENT TYPE: Patent English LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. \_\_\_\_\_ 19990813 EP 1999-202640 Α1 20010214 EP 1075841 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO WO 2000-NL569 20000814 WO 2001012219 A1 20010222 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG 20020502 EP 2000-953578 20000814 A1 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL PRIORITY APPLN. INFO.: EP 1999-202640 A 19990813 WO 2000-NL569 W 20000814 AΒ The invention relates to the use of a protein or a fragment thereof of Streptococcus pneumoniae, its use for the prepn. of a vaccine for the preventive treatment of a S . pneumoniae infection, compns. comprising protease maturation protein of S. pneumoniae or a fragment thereof, vaccines comprising said protein or fragment thereof, use of a nucleic acid sequence encoding for said protein or fragment thereof, vectors wherein the nucleic acid sequence is brought to expression and to recombinant protease maturation protein or a fragment thereof. REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2002 ACS

2000:900503 HCAPLUS ACCESSION NUMBER: DOCUMENT NUMBER: 134:55502 Antibody-based treatment for Streptococcus TITLE: pneumoniae infection INVENTOR(S): Nabors, Gary S.; Briles, David Aventis Pasteur, USA; Uab Research Foundation PATENT ASSIGNEE(S): PCT Int. Appl., 24 pp. SOURCE: CODEN: PIXXD2 DOCUMENT TYPE: Patent English LANGUAGE: FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION: KIND APPLICATION NO. PATENT NO. DATE DATE \_\_\_\_\_ -----------20001221 WO 2000-US16581 20000616 WO 2000076587 Α1 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 2000-939927 20000616 20020410 EP 1194187 A1 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO PRIORITY APPLN. INFO.: US 1999-139524P P 19990616 WO 2000-US16581 W 20000616 The present invention comprises a method of treating a mammal AΒ infected with Streptococcus pneumoniae, which methods comprises administering to the mammal a therapeutically effective amt. of one or more PspA antibodies. Preferably the mammal is a human. REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT HCAPLUS COPYRIGHT 2002 ACS L16 ANSWER 11 OF 25 2000:900481 HCAPLUS ACCESSION NUMBER: 134:55489 DOCUMENT NUMBER: Streptococcus pneumoniae proteins and vaccines TITLE: Adamou, John E.; Choi, Gil H. INVENTOR(S): Med Immune, Inc., USA PATENT ASSIGNEE(S): PCT Int. Appl., 54 pp. SOURCE: CODEN: PIXXD2 Patent DOCUMENT TYPE: LANGUAGE: English FAMILY ACC. NUM. COUNT: PATENT INFORMATION: APPLICATION NO. DATE PATENT NO. KIND DATE 20001221 WO 2000-US15925 20000609 WO 2000076540 A2 WO 2000076540 A3 20010208 AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,

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MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH,
              CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                              20020313
                                              EP 2000-939739
                                                                 20000609
     EP 1185297
                        A2
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
              PT, IE, SI, LT, LV, FI, RO
                                           US 1999-138453P
                                                            Р
                                                                 19990610
PRIORITY APPLN. INFO.:
                                           WO 2000-US15925
                                                             W
                                                                 20000609
     The present invention relates to novel immunogenic
AB
     polypeptides, and fragments thereof, and vaccines for the
     prevention and treatment of pneumococcal infection
     , esp. by Streptococcus pneumoniae. The
     invention also relates to antibodies against the disclosed
     polypeptides, as well as vaccines contg. said polypeptides and
     methods of disease prevention.
L16 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2002 ACS
                           2000:720440 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                           134:37929
                           Protein and DNA sequences of novel proteins from
TITLE:
                           Streptococcus pneumoniae and their uses in
                           diagnosis, therapy and drug screening
                           Altieri, Mario; Domenici, Enrico; Faggioni,
INVENTOR(S):
                           Frederico; Ferrari, Livia; Motti, Harald;
                           Piccoli, Laura; Polissi, Alessandra; Pontiggia,
                           Andrea; Ratti, Emiliangelo; Simon, Daniel
                           Glaxo Group Limited, UK
PATENT ASSIGNEE(S):
                           Brit. UK Pat. Appl., 55 pp.
SOURCE:
                           CODEN: BAXXDU
DOCUMENT TYPE:
                           Patent
LANGUAGE:
                           English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                       KIND
     PATENT NO.
                                              APPLICATION NO.
                                                                 DATE
                              DATE
     GB 2345288
                        Α1
                              20000705
                                              GB 1998-21362
                                                                 19981002
     The invention provides protein and DNA sequences of novel
AΒ
     Streptococcus pneumoniae proteins. The invention further relates to
     the uses of Streptococcus pneumoniae proteins in diagnosis
     and treatment for infections caused by
     Streptococcus pneumoniae, and in drug screening
     designed to identify antimicrobial compds.
L16 ANSWER 13 OF 25
                       HCAPLUS COPYRIGHT 2002 ACS
                           2000:98775 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                           132:162046
TITLE:
                           Sequences of Streptococcus pneumoniae proteins
                           and nucleic acid molecules, and uses thereof in
                           in drug screening, diagnostic, and therapeutic
                           applications
                           Gilbert, Christophe Francois Guy; Hansbro,
INVENTOR(S):
                           Philip Michael
                           Microbial Technics Limited, UK
PATENT ASSIGNEE(S):
SOURCE:
                           PCT Int. Appl., 108 pp.
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Searcher :

308-4994

Shears

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

APPLICATION NO. DATE PATENT NO. KIND DATE \_\_\_\_\_ WO 2000006737 20000210 WO 1999-GB2451 19990727 A2 20000629 WO 2000006737 A3 W: CN, JP, US RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE 20010523 EP 1999-934989 19990727 EP 1100921 A2 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.:

GB 1998-16337 A 19980727 US 1999-125164P P 19990319 WO 1999-GB2451 W 19990727

AB The invention provides sequences of novel protein antigens from type 4 Streptococcus pneumoniae. The invention also provides for the use of the disclosed nucleic acids/proteins as antigens/immunogens, in the diagnosis of Streptococcus infections, and in screening for potential antimicrobial agents.

L16 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1999:577027 HCAPLUS

DOCUMENT NUMBER:

131:198616

TITLE:

Epitope peptides immunogenic against

Streptococcus pneumoniae and their use in

vaccines

INVENTOR(S):

Carlone, George M.; Ades, Edwin W.; Sampson, Jacquelyn S.; Tharpe, Jean A.; Zeiler, Joan

Louise; Westerink, Maria Anna Julia

PATENT ASSIGNEE(S):

The Government of the United States of America,

Represented by the Secretary, USA

SOURCE:

PCT Int. Appl., 59 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	TENT	NO.		KI	ND	DATE			A	PPLI	CATI	ON N	ο.	DATE		
~	00 Å E	101			 1	1000	0010				00-11	C132	<del></del>	1999	0226	
WO	9945	TZI		A	1	エフフフ	OBIO		77	0 19	22-0	3432	U	エフフフ	0220	
	W:	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,
		DE,	DK,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,
		IS,	JP,	ΚE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,
		MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,
		SK,	SL,	ТJ,	TM,	TR,	TT,	UA,	UG,	US,	UZ,	VN,	YU,	ZW,	AM,	ΑZ,
		BY,	·KG,	ΚZ,	MD,	RU,	ТJ,	MT								
	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SL,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,
		DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,
		CF,	CG,	CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	ΤG		
CA	2326	408		A	A	1999	0910		C.	A 19	99-2	3264	80	1999	0226	
ΑU	9927	950		Α	1	1999	0920		Α	U 19	99-2	7950		1999	0226	
BR	9908	476		Α		2000	1205		B:	R 19	99-8	476		1999	0226	

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EP 1060249
                                            EP 1999-908543
                             20001220
                                                             19990226
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
             PT, IE, FI
                                         US 1998-76565P
                                                          P 19980302
PRIORITY APPLN. INFO .:
                                         WO 1999-US4326
                                                          W 19990226
AΒ
     Peptides are provided which immunospecifically bind to monoclonal
     antibodies specific for the 37-kDa pneumococcal surface adhesion A
     protein (PsaA) of Streptococcus pneumoniae of the invention, and
     that are immunogenic against Streptococcus pneumoniae infection.
     Also provided are vaccines comprising such immunogenic
     polypeptides, and methods of conferring protective immunity
     against Streptococcus pneumoniae
     infection by administering therapeutic compns.
     comprising the immunogenic peptides of the invention.
     Also provided are methods of detecting the presence of Streptococcus
     pneumoniae in a sample using antibodies or antigens, and methods of
     preventing and treating Streptococcus pneumoniae infection in a
     subject. In addn. a phage display method of identifying the
     sequence of a peptide potentially capable of eliciting protective
     immunity against a pathogenic microorganism is provided.
REFERENCE COUNT:
                         8
                                THERE ARE 8 CITED REFERENCES AVAILABLE FOR
                                THIS RECORD. ALL CITATIONS AVAILABLE IN
                                THE RE FORMAT
L16 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2002 ACS
                         1999:511257 HCAPLUS
ACCESSION NUMBER:
                         131:154473
DOCUMENT NUMBER:
                         Streptococcus pneumoniae lipidated PsaA protein,
TITLE:
                         a chimeric DNA molecule encoding it, its
                         recombinant production, isolation and
                         purification, and its use in a vaccine for the
                         prevention and treatment of infection
                         Ades, Edwin W.; Carlone, George M.; De Barun, K.; Sampson, Jacquelyn S.; Huebner, Robert C.
INVENTOR(S):
                         Center for Disease Control and Prevention, USA
PATENT ASSIGNEE(S):
                          PCT Int. Appl., 40 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                                            APPLICATION NO.
     PATENT NO.
                      KIND
                            DATE
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                            _____
                                            ______
     WO 9940200
                       A1
                            19990812.
                                            WO 1999-US379
                                                              19990114
                         AU AZ BA BB. BG. BR. BY. CA. CH. CN. CU. CZ
                 ΛM Λπ
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	w:	ΑL,	ΑM,	ΑT,	ΑU,	AZ,	BA,	BB,	BG,	BK,	BI,	$CA_{\bullet}$	CH,	CN,	CU,	$C_{\Delta_{I}}$
		DE,	DK,	EE,	ES,	FΙ,	GB,	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,
		JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,
		MK,	MN,	MW,	MX,	NO,	ΝZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,
		SL,	ТJ,	TM,	TR,	TT,	UA,	UG,	US,	UZ,	VN,	YU,	ZW,	ΑM,	ΑZ,	BY,
		KG,	ΚZ,	MD,	RU,	ТJ,	TM									
	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SZ,	UG,	ZW,	AT,	BE,	CH,	CY,	DE,	DK,
		ES,	FI,	FR,	GB,	GR,	ΙE,	ΙT,	LU,	MC,	NL,	PT,	SE,	BF,	ΒJ,	CF,
		CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG			
CA	2319	404		$\mathbf{A}$	A.	1999	0812		C	A 19	99-2	3194	04	1999	0114	
ΑU	9923	131	•	Α	1 :	1999	0823		A	U 19	99-2	3131		1999	0114	
EΡ	1053	329		Α	1 :	2000	1122		E	P 19	99-9	0301	1	1999	0114	
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,

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PT, IE, FI
    BR 9909097
                                 20001205
                                                  BR 1999-9097
                                                                      19990114
                          Α
                                                                      19990114
                           T2
                                 20020219
                                                  JP 2000-530614
     JP 2002505083
                                               US 1998-17782
                                                                     19980203
PRIORITY APPLN. INFO.:
                                                                  Α
                                               WO 1999-US379
                                                                  W
                                                                     19990114
AΒ
     The invention provides a chimeric DNA mol. contg. the first 52 amino
     acids of Borrelia burgdorferi gene ospA lipoprotein (including the
     signal peptide) fused to the mature form of Streptococcus pneumoniae
     gene psaA pneumococcal surface protein A (PsaA, previously known as
     pneumococcal fimbrial protein A). The invention also provides an
     expression vector contg. the chimeric DNA mol., and the use of the
     vector for recombinant prodn. of lipidated PsaA proteins. The
     invention further provides purifn. methods used to obtain the
     recombinant PsaA proteins, and use of these proteins in immunol.
     compns.
               Also provided are vaccines comprising immunogenic lipidated
     PsaA proteins and methods of use of such vaccines in the
     prevention and treatment of S.
     pneumoniae infection. The sequence of the
     chimeric DNA mol. used in the recombinant prodn. of lipidated PsaA
     proteins was included in the invention.
REFERENCE COUNT:
                             10
                                    THERE ARE 10 CITED REFERENCES AVAILABLE
                                    FOR THIS RECORD. ALL CITATIONS AVAILABLE
                                    IN THE RE FORMAT
                         HCAPLUS COPYRIGHT 2002 ACS
L16 ANSWER 16 OF 25
                             1999:468470 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                             131:98516
TITLE:
                             Essential Streptococcus pneumoniae genes and
                             methods for screening for antibacterial agents
                             Youngman, Philip; Fritz, Christian; Murphy,
INVENTOR(S):
                             Christopher; Guzman, Luz-Maria
                             Millennium Pharmaceuticals, Inc., USA
PATENT ASSIGNEE(S):
SOURCE:
                             PCT Int. Appl., 124 pp.
                             CODEN: PIXXD2
DOCUMENT TYPE:
                             Patent
                             English
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                                                  APPLICATION NO.
                                                                      DATE
     PATENT NO.
                         KIND
                                 DATE
                                                  WO 1998-US27918
                                                                      19981230
     WO 9933871
                          A2
                                 19990708
                                 19991223
     WO 9933871
                          Α3
              AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY,
               KG, KZ,
                        MD, RU, TJ, TM
               GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
          RW: GH, GM,
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AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,

CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

19990708

19990719

20001011

20020212

CA 2315252

AU 9920243

EP 1042361

JP 2002504314

AΑ

**A1** 

A1

PT, IE, FI

CA 1998-2315252

AU 1999-20243

EP 1998-965050

JP 2000-526545

19981230

19981230

19981230

19981230

PRIORITY APPLN. INFO.:

US 1997-70116P P 19971231 WO 1998-US27918 W 19981230

Disclosed are 23 genes, termed "GEP" genes, found in Streptococcus AB pneumoniae, which are located within operons that are essential for survival. Also disclosed is a related essential gene found in Bacillus subtilis. These genes and the polypeptides that they encode, as well as homologs thereof, can be used to identify antibacterial agents for treating bacterial infections such as streptococcal pneumoniae.

L16 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2002 ACS 1999:119779 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

130:193978

TITLE:

Compositions and methods for identifying

compounds for treatment of infection caused by Haemophilus influenzae and Streptococcus

pneumoniae and other bacteria incorporating

choline into cell wall structures

INVENTOR(S):

Weiser, Jeffrey N.

PATENT ASSIGNEE(S):

The Children's Hospital of Philadelphia, USA

SOURCE:

U.S., 31 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE \_\_\_\_\_ US 1997-935396 US 5871951 · A 19990216 19970923

The invention relates to methods of identifying a compd. capable of AΒ disrupting the addn. of choline onto a bacterial cell surface component. The methods comprise incubating a sample of bacteria or bacterial ext. or a bacterial choline kinase in a soln. contg. choline in the presence or absence of a test compd., and assessing the effect of the test compd. on the addn. of choline onto the bacterial cell surface component, wherein a lower level of choline on the cell surface component in the presence of the test compd., compared with the level of choline on the cell surface component in the absence of the test compd., is an indication that the test compd. inhibits the addn. of choline onto the cell surface component. It has been discovered that H. influenzae and S. pneumoniae have a choline kinase which phosphorylates choline to choline phosphate (ChoP) for incorporation into cell wall structures.

REFERENCE COUNT:

36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

HCAPLUS COPYRIGHT 2002 ACS L16 ANSWER 18 OF 25

ACCESSION NUMBER:

1999:42537 HCAPLUS

DOCUMENT NUMBER:

130:106051

TITLE:

Streptococcus pneumoniae gene gidA2

polynucleotides and polypeptides

INVENTOR(S):

Palmer, Leslie Marie; Fedon, Jason Craig; Lenox, Anna Lisa; Kallender, Howard

PATENT ASSIGNEE(S):

Smithkline Beecham Corporation, USA; Smithkline

Beecham Plc

SOURCE:

Eur. Pat. Appl., 41 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

F	PAT	ENT	NO.		KIN	1D	DATE			A	PPLI	CATI	ON NO	ο.	DATE		
• -						-	1000			_			05000		10000	2020	
E	SP	8891	32		A2	-	1999	0107		E	P 19	98-3	05208	3	19980	1630	
F	ΞP	8891	32		A3	3	2002	0320									
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙT,	LI,	LU,	NL,	SE,	MC,
			PT,	ΙE,	SI,	LT,	LV,	FI,	RO								
	CA	2236	441		A.	A	1999	0101		C.	A 19	98-2	23644	41	19980	0629	
j	JΡ	1113	7266		A2	2	1999	0525		J	P 19	98-2	23539	9	19980	701	•
Ċ	JΡ	2000	05089	90	A2	2	2000	0222		J	P 19	99-2	12084	4	19980	701	
PRIOR	ΙΤΥ	APP	LN.	INFO.	:				ı	US 1	997-	5137	8 P	P	19970	701	
									,	JP 1	998-	2235	39	A3	19980	701	

AΒ The invention provides gidA2 polypeptides and polynucleotides encoding gidA2 polypeptides and methods for producing such polypeptides by recombinant techniques. Full-length gene gidA2 from Streptococcus pneumoniae encodes a protein 444 amino acids in length. Also provided are expression systems for prodn. of gidA2 polypeptides, diagnosis and treatment methods for diseases, computer-readable media for homol. identification and assembly, and methods for utilizing gidA2 polypeptides to screen for antibacterial compds.

HCAPLUS COPYRIGHT 2002 ACS L16 ANSWER 19 OF 25

ACCESSION NUMBER:

1999:42535 HCAPLUS

DOCUMENT NUMBER:

130:106049

TITLE:

Streptococcus pneumoniae gene gidB

polynucleotides and polypeptides

INVENTOR(S):

Kallender, Howard

PATENT ASSIGNEE(S):

Smithkline Beecham Corporation, USA; Smithkline

Beecham Plc

SOURCE:

Eur. Pat. Appl., 23 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

P.	ΑT	ENT	NO.		KI	ND	DATE			A	PPLI	CATI	ON NO	ο.	DATE		
_		0001			·		1999	0107		-	D 10	98-3	0510	2	19980	1630	
_	_	8891				2				Ŀ	r 19	90-3	0516.	,	19900	050	
E	Ρ	8891	L30		A.	3	2002	0320									
		R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙΤ,	LI,	LU,	NL,	SE,	MC,
			PT,	ΙE,	SI,	LT,	LV,	FI,	RO								
Ū	S	5866	366		Α		1999	0202		U	S 19	97-8	8663	3	19970	701	
C	Α	2236	6459		A	Ą	1999	0101		C.	A 19	98-2	2364	59	19980	630	
J	P	1113	37267		A:	2	1999	0525		J	P 19	98-2	2354	2	19980	701	
บ	S	6207	7449		B.	1	2001	0327		U	S 19	98-2	1308	1	19981	216	
U	S	6214	1346		₿.	1	2001	0410		U	S 19	98-2	1297	9	19981	216	
PRIORI	ΤY	APE	PLN.	ENFO	. :					US 1	997-	8866	33	Α	19970	701	
AB T	he	inv	renti	on p	rovi	des	gidB	pol	ypep	tide	s an	d po	lynu	cle	otides	3	
е	nc	odir	ng gio	dB po	olyp	epti	des	and i	neth	ods	for	prod	ucin	g sı	ıch		

polypeptides by recombinant techniques. Full-length gene gidB from Streptococcus pneumoniae encodes a protein 237 amino acids in length. Also provided are expression systems for prodn. of qidB polypeptides, diagnosis and treatment methods for diseases, computer-readable media for homol. identification and assembly, and methods for utilizing gidB polypeptides to screen for antibacterial compds.

L16 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1999:42533 HCAPLUS

DOCUMENT NUMBER:

130:106047

TITLE:

Streptococcus pneumoniae gene gidAl polynucleotides and polypeptides

INVENTOR(S):

Palmer, Leslie Marie; Fedon, Jason C.; Lenox, Anna Lisa; Wang, Min; Jaworski, Deborah D.;

Kallender, Howard; Burnham, Martin

PATENT ASSIGNEE(S):

Smithkline Beecham Corporation, USA; Smithkline

Beecham Plc

SOURCE:

Eur. Pat. Appl., 44 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PA	TENT	NO.		KI	ND	DATE			A.	PPL	ICATI	ON NO	Э.	DATE		
	ĔΡ	8891	28		A	2	1999	0107		E	P 1	998-3	0517	4	1998	0630	
•	ΕP	8891			A.	-	2002										
		R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	, IT,	LI,	LU,	NL,	SE,	MC,
			PT,	ΙE,	SI,	LT,	LV,	FΙ,	RO								
	US	6238	882		B	1	2001	0529		Ų	S 1	998-1	0406	8	1998	0624	
	CA	2236	425	-	Αź	4	1999	0101		C	A 1	998-2	2364	25	1998	0629	
	JP	1113	7268		A:	2	1999	0525		J.	P 1	998-2	2354	3	1998	0701	
	JP	2000	21009	93	A:	2	2000	0802		J:	P 2	000-5	3626		1998	0701	
PRIOR	RITY	APP	LN.	INFO	. :				į	US 1	997	-5137	9P	Ρ	1997	0701	
										TP 1	998	~2235	43	Α3	19980	0701	

The invention provides gidAl polypeptides and polynucleotides AΒ encoding gidAl polypeptides and methods for producing such polypeptides by recombinant techniques. Full-length gene gidA1 from Streptococcus pneumoniae encodes a protein 637 amino acids in length. Also provided are expression systems for prodn. of gidAl polypeptides, diagnosis and treatment methods for diseases, computer-readable media for homol. identification and assembly, and methods for utilizing gidAl polypeptides to screen for antibacterial compds.

L16 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1998:197634 HCAPLUS

DOCUMENT NUMBER:

128:278969

TITLE:

Compositions and methods for treatment of

infection caused by Haemophilus influenzae and

Streptococcus pneumoniae

INVENTOR(S):

Weiser, Jeffrey N.

PATENT ASSIGNEE(S):

Children's Hospital of Philadelphia, USA

SOURCE:

PCT Int. Appl., 54 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

APPLICATION NO. DATE PATENT NO. KIND DATE \_\_\_\_\_ WO 9812346 19980326 WO 1997-US16807 19970923 A1

W: AU, CA, JP

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE

19980324 CA 1997-2196502 19970131 CA 2196502 AΑ AU 9744907 A1 19980414 AU 1997-44907 19970923 PRIORITY APPLN. INFO.: US 1996-26940P P 19960923 WO 1997-US16807 W 19970923

The invention relates to a method of identifying a compd. capable of AB disrupting the addn. of choline onto a bacterial cell surface component comprising incubating a sample of bacteria in a soln. contg. choline in the presence or absence of a test compd., and assessing the effect of the test compd. on the addn. of choline onto the bacterial cell surface component, wherein a lower level of choline on the cell surface component in the presence of the test compd., compared with the level of choline on the cell surface component in the absence of the test compd., is an indication that the test compd. inhibits the addn. of choline onto the cell surface component.

L16 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1997:679183 HCAPLUS

DOCUMENT NUMBER:

127:356941

TITLE:

Genomic DNA sequences of Streptococcus pneumoniae strain 0100993, their predicted

protein products, and their diagnostical and

therapeutical uses

INVENTOR(S):

Black, Michael Terrance; Hodgson, John Edward; Knowles, David Justin Charles; Nicholas, Richard

Oakley; Stodola, Robert King

PATENT ASSIGNEE(S):

Smithkline Beecham Corp., USA; Smithkline Beecham PLC; Black, Michael Terrance; Hodgson, John Edward; Knowles, David Justin Charles; Nicholas, Richard Oakley; Stodola, Robert King

SOURCE:

PCT Int. Appl., 353 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9737026	A1	19971009	WO 1997-US5306	19970401
W: JP, US				
RW: AT, BE,	CH, DE	, DK, ES,	FI, FR, GB, GR, IE, IT,	LU, MC, NL,
PT, SE				
EP 907738	A1	19990414	EP 1997-920002	19970401
R: BE, CH,	DE, DK	, FR, GB,	IT, LI, NL	
JP 2000511769	T2	20000912	JP 1997-535535	19970401
PRIORITY APPLN. INFO	. :		US 1996-14690P P	19960402
-			US 1996-25788P P	19960822

WO 1997-US5306 W 19970401

AΒ The genomic DNA sequences of Streptococcus pneumoniae strain 0100993 are isolated and the amino acid sequences of the predicted polypeptides are deduced from open reading frames (ORF). Claimed are the antibodies against the polypeptides, methods of identifying the compds. that interact with the polypeptides, methods of identifying antimicrobial compds., and clin. use of the polypeptides.

L16 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1997:248926 HCAPLUS

DOCUMENT NUMBER:

126:311795

TITLE:

Immunization with a plasmid expressing

pneumococcal surface protein A (PspA) can elicit

protection against fatal infection with

Streptococcus pneumoniae

AUTHOR(S):

McDaniel, L. S.; Loechel, F.; Benedict, C.; Greenway, T.; Briles, D. E.; Conry, R. M.;

Curiel, D. T.

CORPORATE SOURCE:

Bacterial Pathogenesis Lab., Univ. Alabama,

Birmingham, AL, USA

SOURCE:

Gene Therapy (1997), 4(4), 375-377

CODEN: GETHEC; ISSN: 0969-7128

PUBLISHER:

Stockton DOCUMENT TYPE: Journal English LANGUAGE:

Pneumococcal surface protein A (PspA) is a protection-eliciting AB protein of Streptococcus pneumoniae. We obsd. that immunization of BALB/c mice with a plasmid expressing PspA significantly protected the mice from lethal challenge with S. pneumoniae when compared to control mice that received injections of the plasmid vector alone. The plasmid construct expressing PspA has been designated pKSD2601. Mice immunized i.m. with pKSD2601 had a mean log of colony-forming units of 2.97 .+-. 0.25 pneumococci circulating in their blood at 24 h after challenge as compared with control mice that had a mean log of colony-forming units of 4.95 .+-. 0.59. Those mice with lower nos. of pneumococci subsequently survived the challenge. Given the quant. nature and ultimate end point (ie live vs. dead) our mouse model should be useful in working out optimum expression of bacterial genes for DNA immunization.

HCAPLUS COPYRIGHT 2002 ACS L16 ANSWER 24 OF 25

ACCESSION NUMBER:

1995:813133 HCAPLUS

DOCUMENT NUMBER:

123:218379

TITLE:

Treatment of gram-positive bacterial infections with bactericidal/permeability protein BPI and its fragments alone or in combination with

antibiotics

INVENTOR(S):

Horowitz, Arnold; Lambert, Lewis H., Jr.;

Little, Roger G., II

PATENT ASSIGNEE(S):

Xoma Corp., USA

SOURCE:

PCT Int. Appl., 260 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

12

PATENT INFORMATION:

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KIND
                             DATE
                                              APPLICATION NO.
                                                                DATE
     PATENT NO.
                       ____
                              _____
                                                                19950117
                                              WO 1995-US656
     WO 9519180
                              19950720
                        A1
             AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI,
              SK, TJ, TT, UA, UZ
         RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,
              LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR,
              NE, SN, TD, TG
                              19980331
                                              US 1994-209762
                                                                19940311
     US 5733872
                        Α
                              19950801
                                              AU 1995-16822
                                                                19950113
                        Α1
     AU 9516822
                        B2
                              19990318
     AU 703192
                        Α
                                              ZA 1995-249
                                                                19950113
     ZA 9500249
                              19950808
                        Α
                              19950904
                                              ZA 1995-248
                                                                19950113
     ZA 9500248
                              19970122
                                              EP 1995-908545
                                                                19950113
     EP 754050
                        Α1
                              20020626
     EP 754050
                        .B1
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL,
              PT, SE
                        T2
                              19970826
                                              JP 1995-519190
                                                                19950113
     JP 09508359
                                           US 1994-183222
                                                            Α
                                                                19940114
PRIORITY APPLN. INFO.:
                                          US 1994-209762
                                                             Α
                                                                19940311
                                          US 1994-274299
                                                             A 19940711
                                          US 1993-30644
                                                             A2 19930312
                                          US 1993-93202
                                                             B2 19930715
                                          WO 1994-US10427
                                                             W
                                                               19940915
                                          WO 1995-US656
                                                             W 19950117
AB Gram-pos. bacterial infections are treated by administration of a
     bactericidal/permeability-inducing (BPI) protein product alone, or
     in combination with an antibiotic. BPI protein product alone has a
     bactericidal or growth inhibitory effect on selected gram-pos.
     organisms. BPI protein product also increases the susceptibility of
     gram-pos. organisms to antibiotics and can even reverse resistance
     of gram-pos. organisms to antibiotic.
                       HCAPLUS COPYRIGHT 2002 ACS
L16 ANSWER 25 OF 25
                          1995:480300 HCAPLUS
ACCESSION NUMBER:
                          124:45721
DOCUMENT NUMBER:
                          Method of treating pulmonary disease states with
TITLE:
                          non-naturally occurring amphipathic peptides
                          Jaynes, Jesse M.; Julian, Gordon R.
INVENTOR(S):
                          Demeter Biotechnologies, Ltd., USA
PATENT ASSIGNEE(S):
                          PCT Int. Appl., 53 pp.
SOURCE:
                          CODEN: PIXXD2
DOCUMENT TYPE:
                          Patent
LANGUAGE:
                          English
FAMILY ACC. NUM. COUNT:
                          10
PATENT INFORMATION:
     PATENT NO.
                       KIND
                              DATE
                                              APPLICATION NO.
                                                                DATE
     _____
     WO 9428921
                                                                19940602
                        A1
                              19941222
                                              WO 1994-US6176
         W: AU, CA, FI, JP, KR, NO, NZ
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT,
              SE
     AU 9470502
                        A1
                              19950103
                                              AU 1994-70502
                                                                19940602
                                                                19950601
     US 5744445
                              19980428
                                              US 1995-457798
                        Α
PRIORITY APPLN. INFO.:
                                           US 1993-39620
                                                                19930604
                                                             Α
```

WO 1994-US6176 W 19940602 A method of treating pulmonary disease states, e.g., a disease state selected from the group consisting of: cystic fibrosis, neoplasias, bronchogenic cancers, pneumonia, bronchitis, bronchopulmonary viral infections, and bronchopulmonary microbial infections, comprises delivery of an amphipathic non-naturally occurring peptide to an appropriate corporeal site, e.g, pulmonary and/or gastrointestinal loci, to effectively treat such diseases. A method is claimed for treating cystic fibrosis by delivery of lytic, amphipathic non-naturally occurring peptides to pulmonary loci, thereby effecting treatment of bronchopulmonary microbial infections assocd. with cystic fibrosis through lysis of pathogenic bacteria. Peptides delivered to a gastrointestinal locus preferably are non-lytic, so as not to affect normal gastrointestinal flora, and preferably are chem. modified to confer enhanced proteolytic resistance for an oral method of delivery. Peptides delivered to a pulmonary locus advantageously exhibit lytic activity and do not require chem. modification for proteolytic resistance. The delivery of the

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peptide to a pulmonary locus may involve a nebulizer device.
     (FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     DICST EPLUS, JAPIO' ENTERED AT 14:58:04 ON 31 JUL 2002)
           206 SEA ABB=ON PLU=ON L16
L17
             90 SEA ABB=ON PLU=ON L17(S)(INHIBIT? OR ANTAGON? OR
L18
                INTERFER?)
L19
             75 DUP REM L18 (15 DUPLICATES REMOVED)
             33 SEA ABB=ON PLU=ON L19 AND (MEDICAMENT OR MEDICINE OR
L203
                DRUG OR PHARMAC?)
             27 SEA ABB=ON PLU=ON L19 AND (METHOD OR TECHNIQUE OR
                PROCESS OR PROCEDUR?)
             49 SEA ABB=ON PLU=ON L20 OR L21
                        MEDLINE
L22 ANSWER 1 OF 49
ACCESSION NUMBER:
                    2002152896
                                   MEDLINE
                               PubMed ID: 11796344
DOCUMENT NUMBER:
                    21654663
TITLE:
                    Susceptibilities to telithromycin and six other
                    agents and prevalence of macrolide resistance due to
                    L4 ribosomal protein mutation among 992 Pneumococci
                    from 10 central and Eastern European countries.
```

AUTHOR:

Nagai Kensuke; Appelbaum Peter C; Davies Todd A; Kelly Linda M; Hoellman Dianne B; Andrasevic Arjana Tambic; Drukalska Liga; Hryniewicz Waleria; Jacobs Michael R; Kolman Jana; Miciuleviciene Jolanta; Pana Marina; Setchanova Lena; Thege Marianne Konkoly; Hupkova Helena; Trupl Jan; Urbaskova Pavla

CORPORATE SOURCE:

Department of Pathology, Hershey Medical Center,

Hershey, Pennsylvania 17033, USA.

SOURCE: ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (2002 Feb) 46

(2) 371-7.

Journal code: 0315061. ISSN: 0066-4804.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE) DOCUMENT TYPE:

LANGUAGE: English

Priority Journals FILE SEGMENT:

ENTRY MONTH: 200205

Entered STN: 20020312 ENTRY DATE:

Last Updated on STN: 20020509 Entered Medline: 20020508

The macrolide and levofloxacin susceptibilities of 992 isolates of AΒ Streptococcus pneumoniae from clinical specimens collected in 1999 and 2000 were determined in 10 centers in Central and Eastern European countries. The prevalences of penicillin G-intermediate (MICs, 0.125 to 1 microg/ml) and penicillin-resistant (MICs, < or =2microg/ml) Streptococcus pneumoniae isolates were 14.3 and 16.6%, respectively. The MICs at which 50% of isolates are inhibited (MIC(50)s) and the MIC(90)s of telithromycin were 0.016 and 0.06 microg/ml, respectively; those of erythromycin were 0.06 and >64 microg/ml, respectively; those of azithromycin were 0.125 and >64 microg/ml, respectively; those of clarithromycin were 0.03 and >64 microg/ml, respectively; and those of clindamycin were 0.06 and >64 microg/ml, respectively. Erythromycin resistance was found in 180 S. pneumoniae isolates (18.1%); the highest prevalence of erythromycin-resistant S. pneumoniae was observed in Hungary (35.5%). Among erythromycin-resistant S. pneumoniae isolates, strains harboring erm(B) genes (125 strains [69.4%]) were found to be predominant over strains with mef(E) genes (25 strains [13.4%]), L4 protein mutations (28 strains [15.6%]), and erm(A) genes (2 strains [1.1%]). Similar pulsed-field gel electrophoresis patterns suggested that some strains containing L4 mutations from the Slovak Republic, Bulgaria, and Latvia were clonally related. Of nine strains highly resistant to levofloxacin (MICs, >8 microg/ml) six were isolated from Zagreb, Croatia. Telithromycin at < or =0.5 microg/ml was active against 99.8% of S. pneumoniae isolates tested and may be useful for the treatment of respiratory tract infections caused by macrolide-resistant S. pneumoniae isolates.

L22 ANSWER 2 OF 49 MEDLINE

ACCESSION NUMBER:

1999275816 MEDLINE

DOCUMENT NUMBER:

99275816 PubMed ID: 10348060

TITLE:

Drug-resistant Streptococcus pneumoniae:

rational antibiotic choices.

AUTHOR:

Jacobs M R

CORPORATE SOURCE:

Department of Pathology, Case Western Reserve

University School of Medicine, University Hospitals

of Cleveland, Ohio 44106, USA.

SOURCE:

AMERICAN JOURNAL OF MEDICINE, (1999 May 3) 106 (5A)

19S-25S; discussion 48S-52S. Ref: 52 Journal code: 0267200. ISSN: 0002-9343.

PUB. COUNTRY:

United States

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE:

English

FILE SEGMENT:

Abridged Index Medicus Journals; Priority Journals

199906

ENTRY MONTH: ENTRY DATE:

Entered STN: 19990614

Last Updated on STN: 19990614 Entered Medline: 19990603

AB Increasingly, Streptococcus pneumoniae with reduced susceptibility to penicillin is becoming a healthcare concern, not only because of the high prevalence of infections caused by this pathogen but also because of the rate at which resistance has progressed. The incidence of penicillin resistance in strains of S. pneumoniae approaches 40% in some areas of the United States, and the incidence of high-level resistance has increased by 60-fold during the past 10

years. With the exception of meningitis and otitis media, there is no conclusive evidence that the acquisition of resistance by S. pneumoniae to beta-lactam antibiotics incurs greater morbidity and mortality in infections caused by this pathogen. However, if the current trends of resistance patterns continue, one can expect the morbidity and mortality to increase. The mechanism of beta-lactam resistance of S. pneumoniae involves genetic mutations which alter penicillin-binding protein structure, resulting in a decreased affinity for all beta-lactam antibiotics. In the treatment of infections caused by S. pneumoniae, it should not be assumed that nonsusceptibility to beta-lactam antibiotics correlates with clinical ineffectiveness of these agents. On the contrary, the recommended therapy for nonmeningeal pneumococcal infections (e.g., pneumonia, sepsis, acute otitis media) includes a beta-lactam antibiotic: penicillin G, amoxicillin, amoxicillin/clavulanate, cefuroxime, cefotaxime, or ceftriaxone. Recommended therapy for meningitis is cefotaxime or ceftriaxone, with the addition of vancomycin until susceptibility is known. These agents are recommended because of their ability to achieve serum/tissue concentrations greater than the minimum inhibitory concentrations (MICs) of these agents against penicillin-susceptible, penicillin-intermediate, and most penicillin-resistant strains (e.g., penicillin G, cefotaxime, ceftriaxone, amoxicillin, amoxicillin/clavulanate, and cefuroxime), or their ability to provide adequate concentrations in cerebrospinal fluid (e.g., cefotaxime, ceftriaxone).

L22 ANSWER 3 OF 49 MEDLINE

1999265127 ACCESSION NUMBER: MEDLINE

PubMed ID: 10332723 DOCUMENT NUMBER: 99265127

Otitis media: the chinchilla model. TITLE:

Giebink G S AUTHOR:

CORPORATE SOURCE: Otitis Media Research Center, University of Minnesota

School of Medicine, Minneapolis 55455, USA.

MICROBIAL DRUG RESISTANCE, (1999 Spring) 5 (1) 57-72. SOURCE:

Ref: 157

Journal code: 9508567. ISSN: 1076-6294.

United States

Journal; Article; (JOURNAL ARTICLE) DOCUMENT TYPE:

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: English

Priority Journals FILE SEGMENT:

ENTRY MONTH: 199907

PUB. COUNTRY:

ENTRY DATE: Entered STN: 19990730

Last Updated on STN: 19990730

Entered Medline: 19990720

Streptococcus pneumoniae infection and AB

disease have been modeled in several animal species including infant and adult mice, infant and adult rats, infant Rhesus monkeys, and adolescent and adult chinchillas. Most are models of sepsis arising from intravenous or intraperitoneal inoculation of bacteria, and a few were designed to study disease arising from intranasal infection. Chinchillas provide the only animal model of middle ear pneumococcal infection in which the disease can be produced by very small inocula injected into the middle ear (ME) or intranasally, and in which the disease remains localized to the ME in most cases. This model, developed at the University of Minnesota in 1975, has been

used to study pneumococcal pathogenesis at a mucosal site, immunogenicity and efficacy of pneumococcal capsular polysaccharide (PS) vaccine antigens, and the kinetics and efficacy of antimicrobial drugs. Pathogenesis experiments in the chinchilla model have revealed variation in ME virulence among different pneumococcal serotypes, enhancement of ME infection during concurrent intranasal influenza A virus infections, and natural resolution of pneumococcal otitis media (OM) without intervention. Research has explored the relative contribution of pneumococcal and host products to ME inflammation. Pneumococcal cell wall components and pneumolysin have been studied in the model. Host inflammatory responses studied in the chinchilla ME include polymorphonuclear leukocyte oxidative products, hydrolytic enzymes, cytokine and eicosanoid metabolites, and ME epithelial cell adhesion and mucous glycoprotein production. Both clinical (tympanic membrane appearance) and histopathology (ME, Eustachian tube, inner ear) endpoints can be quantified. Immunologic and inflammatory studies have been facilitated by the production of affinity-purified antichinchilla immunoglobulin G (IgG), IgM, and secretory IgA polyclonal antibody reagents, and the identification of cross-reactivity between human and chinchilla cytokines, and between guinea pig and chinchilla C3. Alteration of ME mucosa by pneumococcal neuraminidase and alteration of ME epithelial cell (MEEC) surface carbohydrates during intranasal pneumococcal infection have been demonstrated. Pathogenesis studies have been aided by cultured chinchilla MEEC systems, in which the ability of platelet activating factor and interleukin (IL)-1 beta to stimulate epithelial mucous glycoprotein synthesis has recently been demonstrated. Because chronic OM with effusion is characterized by presence of large amounts of mucous glycoprotein in the ME, pneumococcus may have an important role in both acute and chronic ME disease. Both unconjugated PS and PS-protein-conjugated vaccines are immunogenic after intramuscular administration without adjuvant in chinchillas. Passive protection studies with human hyperimmune immunoglobulin demonstrated that anti-PS IgG alone is capable of protecting the chinchilla ME from direct ME challenge with pneumococci. Active PS immunization studies demonstrated protection following direct ME and intranasal pneumococcal challenge with and without concurrent influenza A virus infection. An attenuated influenza A virus vaccine also showed protection for pneumococcal OM. Antimicrobial treatment of acute OM has been based almost exclusively on empirical drug use and clinical trials without a foundation of ME pharmacokinetics . Studies in the chinchilla model have started to bring a rational basis to drug selection and dosing. Microassays have been developed using high-pressure liquid chromatography for many relevant drugs. Studies have explored the in vivo ME response in pneumococcal OM to antimicrobial drugs at supra- and sub-minimum inhibitory concentration (MIC), the effect of concurrent influenza A virus infection on ME drug penetration, and the effect of treatment on sensorineural hearing loss produced by pneumococcal OM.

L22 ANSWER 4 OF 49 MEDLINE

ACCESSION NUMBER: 1999013576 MEDLINE

DOCUMENT NUMBER: 99013576 PubMed ID: 9797230

TITLE: In vitro and in vivo antibacterial activities of

OPC-20011, a novel parenteral broad-spectrum

2-oxaisocephem antibiotic.

AUTHOR: Matsumoto M; Tamaoka H; Ishikawa H; Kikuchi M

CORPORATE SOURCE: Microbiological Research Institute, Otsuka

Pharmaceutical Co., Ltd., Tokushima City, Tokushima

Prefecture 771-0192, Japan..

m.matsumoto@research.otsuka.co.jp

SOURCE: ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (1998 Nov) 42

(11) 2943-9.

Journal code: 0315061. ISSN: 0066-4804.

PUB. COUNTRY:

United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199812

ENTRY DATE: Entered STN: 19990115

Last Updated on STN: 19990115 Entered Medline: 19981204

OPC-20011, a new parenteral 2-oxaisocephem antibiotic, has an oxygen ΑB atom at the 2- position of the cephalosporin frame. OPC-20011 had the best antibacterial activities against gram-positive bacteria, including methicillin-resistant Staphylococcus aureus (MRSA), Enterococcus faecalis, and penicillin-resistant Streptococcus pneumoniae: MICs at which 90% of the isolates were inhibited were 6.25, 6.25, and 0.05 microg/ml, respectively. Its activity is due to a high affinity of the penicillin-binding protein 2' in MRSA, an affinity which was approximately 1,050 times as high as that for flomoxef. Against gram-negative bacteria, OPC-20011 also showed antibacterial activities similar to those of ceftazidime. The in vivo activities of OPC-20011 were comparable to or greater than those of reference compounds in murine models of systemic infection caused by gram-positive and -negative pathogens. OPC-20011 was up to 10 times as effective as vancomycin against MRSA infections in mice. This better in vivo efficacy is probably due to the bactericidal activity of OPC-20011, while vancomycin showed bacteriostatic activity against MRSA. OPC-20011 produced a significant decrease of viable counts in lung tissue at a dose of 2.5 mg/kg of body weight, an efficacy similar to that of ampicillin at a dose of 10 to 20 mg/kg on an experimental murine model of respiratory tract infection caused by non-ampicillin-susceptible S. pneumoniae T-0005. The better therapeutic efficacy of OPC-20011 was considered to be due to its potent antibacterial activity and low affinity for serum proteins of experimental animals (29% in mice and 6.4% in rats).

L22 ANSWER 5 OF 49 MEDLINE

ACCESSION NUMBER: 84112778 MEDLINE

DOCUMENT NUMBER: 84112778 PubMed ID: 6363539

TITLE: Inhibition of antibody responses to phosphocholine by

C-reactive protein.

AUTHOR: Nakayama S; Du Clos T W; Gewurz H; Mold C

CONTRACT NUMBER: AI-16082 (NIAID)

SOURCE: JOURNAL OF IMMUNOLOGY, (1984 Mar) 132 (3) 1336-40.

Journal code: 2985117R. ISSN: 0022-1767.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 198403

ENTRY DATE:

Entered STN: 19900319

Last Updated on STN: 19970203 Entered Medline: 19840323

AΒ C-reactive protein (CRP) is an acute phase serum protein in man that binds to the cell wall C-polysaccharide (PnC) of Streptococcus pneumoniae via phosphocholine (PC) determinants. We have previously shown that in mice CRP increases splenic clearance of PnC-coated autologous erythrocytes and S. pneumoniae, and increases survival after pneumococcal infection. Because CRP alters clearance of particulate PnC antigens, we tested its effect on immunization with pneumococci. Pretreatment of mice with 50 to 200 micrograms CRP 30 min before immunization with serotype 3 S. pneumoniae resulted in dose-dependent inhibition of the antibody response to PC. Both serum hemagglutinin and splenic PFC against PC were decreased in CRP-treated mice tested from 1 to 10 days after injection of antigen. CRP treatment had no effect on the antibody response to the serotype 3 capsular polysaccharide, another T-independent antigen. To determine whether CRP inhibition was related to altered processing of particulate antigen, mice were immunized with horse red blood cells (HRBC) conjugated with PC or PnC and the PFC responses to PC and HRBC were determined. CRP treatment resulted in specific inhibition of the PFC response to PC in both cases without affecting the response to HRBC. These results indicate that inhibition of the antibody response by CRP is not the result of altered antigen localization and processing, and that CRP may prevent immunization

L22 ANSWER 6 OF 49 MEDLINE

84086800 ACCESSION NUMBER:

DOCUMENT NUMBER:

MEDLINE

TITLE:

84086800 PubMed ID: 6418655 Induction of human gamma interferon by structurally

defined polypeptide fragments of group A

streptococcal M protein.

by masking determinants on bacterial or other surfaces.

AUTHOR:

Weigent D A; Beachey E H; Huff T; Peterson J W;

Stanton G J; Baron S

CONTRACT NUMBER:

AI-10085 (NIAID)

AI-13550 (NIAID) EY01715 (NEI)

SOURCE:

INFECTION AND IMMUNITY, (1984 Jan) 43 (1) 122-6.

Journal code: 0246127. ISSN: 0019-9567.

PUB. COUNTRY:

United States

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

198402

ENTRY DATE:

Entered STN: 19900319

Last Updated on STN: 19970203 Entered Medline: 19840215

The presence of interferon (IFN) has been demonstrated AΒ previously (i) in fluids obtained from the middle ears of children with Streptococcus pneumoniae infections

, (ii) from the serum of mice injected intraperitoneally with either S. pneumoniae or Streptococcus pyogenes, and (iii) from human lymphoid cell cultures treated with a variety of bacteria. In this study, we showed that highly purified peptic extracts of three different serotypes of group A streptococcal M protein

(pep M5, pep M6, and pep M24) stimulated human peripheral leukocytes to produce IFN. IFN production was apparent by 10 h and peaked 24 h after exposure. Dose-response experiments indicated that IFN could be detected in cultures treated with concentrations of M protein as low as 6 micrograms/ml, whereas maximum IFN production occurred at a concentration of 200 micrograms/ml. The IFN had antigenic and physicochemical characteristics of IFN-gamma. Preliminary leukocyte fractionation studies revealed that the IFN-producing cell was a nonadherent lymphocyte with receptors for sheep erythrocytes (T cell). Rabbit antisera specific for these structurally defined polypeptide fragments of streptococcal M protein (pep M5, pep M6, and pep M24) blocked IFN induction by each of the polypeptides. The data suggest that the different serotypes of streptococcal M protein may induce IFN by a common structural determinant shared by each of the polypeptide fragments tested.

L22 ANSWER 7 OF 49 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: DOCUMENT NUMBER:

2002:284747 BIOSIS

PREV200200284747

TITLE:

[Potential use of linezolid in the treatment of

infections due to Gram positive cocci.

Original Title: Interet du linezolide pour le

traitement des infections a cocci a Gram positif..

AUTHOR(S):

Kassis-Chikhani, N.; Muller-Serieys, C. (1)

CORPORATE SOURCE:

(1) Laboratoire de Bacteriologie, Groupe Hospitalier

Bichat Claude Bernard, 46 Rue Henri-Huchard, 75018, Paris: claudette.muller@bch.ap-hop-paris.fr France

SOURCE:

Antibiotiques, (Fevrier, 2002) Vol. 4, No. 1 Cahier

1, pp. 38-44. http://www.e2med.com/anti. print.

ISSN: 1294-5501.

DOCUMENT TYPE:

Article

LANGUAGE: French AB

The incidence of infections with multi-resistant Gram-positive cocci increased significantly during the last decade and bacteria responsible for community acquired infections (S . pneumoniae, S. aureus) became resistant to conventional antibiotics used to treat these infections. In spite of preventive measures, nosocomial infections due to Gram positive cocci continue to increase and therapeutic alternatives are decreasing. Linezolid is a member of a new class of synthetic antimicrobial agents known as oxazolidinones, whose particular mechanism of action consists in inhibiting the initiation of protein synthesis. Its spectrum of in vitro and in vivo activity includes methicillin-resistant S. aureus and coagulase-negative staphylococci (CNS), enterococci especially vancomycin and ampicillin-resistant strains, and penicillin-susceptible and resistant S. pneumoniae. So far no cross-resistance between linezolid and other antimicrobial agents has been detected. Selection of resistant mutants is difficult to obtain in vitro. Pharmacokinetic studies have shown that linezolid was rapidly and completely absorbed. After oral administration of multiple doses of 625 mg of linezolid, peak plasma concentration (Cmax) reached 18 mg/l and minimum plasma concentration was close to 4 mg/l at steady-state. The elimination half-life was about 5 hours and the bioavailability reached 100%. At steady-state, 30% of the dose was excreted intact in the urine. Phase III trials in skin and soft tissue infections due to Gram

> 308-4994 Searcher Shears

positive cocci, nosocomial pneumonia and experimental endocarditis showed a similar efficacy and safety profile of linezolid and reference treatments.

L22 ANSWER 8 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002097162 EMBASE

TITLE: Potential use of linezolid in the treatment of

infections due to Gram positive cocci.

AUTHOR: Kassis-Chikhani N.; Muller-Serieys C.

CORPORATE SOURCE: C. Muller-Serieys, Groupe Hosp. Bichat Claude

Bernard, Laboratoire de Bacteriologie, 46 Rue

Henri-Huchard, 75018 Paris, France. claudette.muller@bch.ap-hop-paris.fr

SOURCE: Antibiotiques, (2001) 4/1 I (38-44).

Refs: 57

ISSN: 1294-5501 CODEN: ANTBFQ

COUNTRY: France

DOCUMENT TYPE: Journal; Article FILE SEGMENT: 004 Microbiology 030 Pharmacology

037 Drug Literature Index

LANGUAGE: English SUMMARY LANGUAGE: English

AB The incidence of infections with multi-resistant Gram-positive cocci

increased significantly during the last decade and bacteria

responsible for community acquired infections (S

. pneumoniae, S. aureus) became resistant to conventional antibiotics used to treat these infections. In spite of preventive measures, nosocomial infections due to Gram positive cocci continue to increase and therapeutic alternatives

cocci continue to increase and therapeutic alternatives are decreasing. Linezolid is a member of a new class of synthetic antimicrobial agents known as oxazolidinones, whose particular mechanism of action consists in inhibiting the initiation of protein synthesis. Its spectrum of in vitro and in vivo activity includes methicillin-resistant S. aureus and coagulase-negative staphylococci (CNS), enterococci especially

vancomycin and ampicillin-resistant strains, and penicillin-susceptible and resistant S. pneumoniae. So far no cross-resistance between linezolid and other antimicrobial agents has been detected. Selection of resistant mutants is difficult to obtain in vitro. **Pharmacokinetic** studies have shown that

linezolid was rapidly and completely absorbed. After oral administration of multiple doses of 625 mg of linezolid, peak plasma

concentration of multiple doses of 625 mg of linezolid, peak plasma concentration (Cmax) reached 18 mg/l and minimum plasma concentration was close to 4 mg/l at steady-state. The elimination half-life was about 5 hours and the bioavailability reached 100%. At

steady-state, 30% of the dose was excreted intact in the urine. Phase III trials in skin and soft tissue infections due to Gram positive cocci, nosocomial pneumonia and experimental endocarditis showed a similar efficacy and safety profile of linezolid and reference treatments.

reference creatments.

L22 ANSWER 9 OF 49 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 92190982 EMBASE

DOCUMENT NUMBER: 1992190982

TITLE: Cefetamet pivoxil: A review of its microbiology,

toxicology, pharmacokinetics and clinical

efficacy.

Cullmann W.; Edwards D.J.; Kissling M.; Kneer J.; AUTHOR: Stoeckel K.; Urwyler H. CORPORATE SOURCE: Department of Clinical Research, F. Hoffmann-La Roche Ltd., Grenzacherstrasse 124, CH-4002 Basel, Switzerland SOURCE: International Journal of Antimicrobial Agents, (1992) 1/4 (175-192). ISSN: 0924-8579 CODEN: IAAGEA COUNTRY: Netherlands DOCUMENT TYPE: Journal; General Review FILE SEGMENT: 004 Microbiology 011 Otorhinolaryngology 015 Chest Diseases, Thoracic Surgery and Tuberculosis 028 Urology and Nephrology 052 Toxicology 030 -Pharmacology 037 Drug Literature Index Adverse Reactions Titles 038 LANGUAGE: English SUMMARY LANGUAGE: English Cefetamet pivoxil is an oral, third-generation cephalosporin whose broad spectrum of antibacterial activity and favorable pharmacokinetic profile make it particularly suitable for the treatment of a wide range of infectious diseases. Cefetamet has high in vitro activity against both gram-positive and gram-negative bacteria that cause a number of respiratory tract and urinary tract infections. These include penicillin-sensitive Streptococcus pneumoniae, Streptococcus spp, Haemophilus influenzae, Moraxella catarrhalis, Escherichia coli, Proteus spp., Klebsiella spp. and Neisseria gonorrhoeae. It is not active against staphylococci, enterococci, Pseudomonas spp. or Bacteroides fragilis but does inhibit most bile-sensitive (oral) Bacteroides spp. Animal toxicology studies indicate that neither cefetamet pivoxil nor the active compound cefetamet have significant teratogenic, mutagenic, photogenic or allergenic potential. Cefetamet is eliminated unchanged in the urine with a half-life of 2.2 h. Volume of distribution approximates the extracellular fluid space (0.3 1/kg), protein binding is minimal (22%) and oral bioavailability of cefetamet pivoxil is approximately 50% when taken with food. No significant drug interactions have been noted to date. The efficacy and tolerability of cefetamet pivoxil have been evaluated in the treatment of gram-positive and gram-negative infections in almost 5,000 patients. In comparative studies, cefetamet pivoxil was at least as effective, and in many cases clinically superior, to most currently recommended antibiotics for

the treatment of urinary tract infections including

phenoxymethylpenicillin in the treatment of

Searcher: Shears 308-4994

gonorrhea and complicated infections in high risk patients. Efficacy

pharyngotonsillitis. Cefetamet pivoxil has been well-tolerated in clinical trials with only 1.2% of patients on standard doses discontinuing therapy prematurely. The most common adverse effects are gastrointestinal (diarrhea, nausea, vomiting) which

has also been demonstrated in acute exacerbations of chronic bronchitis, pneumonia and infections of the ear, nose and throat.

Clinical trials have shown that a 7 day **treatment** period with cefetamet pivoxil is as effective as a 10 day course of

occur in less than 10% of patients. Many current antibiotic treatment regimens involve the administration of three or more daily doses. However, standard doses of cefetamet pivoxil 500 mg twice daily provide unbound plasma concentrations of cefetamet which generally exceed the MIC90 for susceptible organisms throughout the dosing interval and have been demonstrated to be clinically effective. This should result in good compliance with therapy in out-patients. Dosing regimens for cefetamet pivoxil should be adjusted in patients with impaired renal function while standard doses can be given to elderly patients and those with liver disease. Standard doses in children are 10 mg/kg or alternatively, children may receive a dose reduced in proportion to the ratio of their body surface area to that of an adult.

L22 ANSWER 10 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

2001-465364 [50] WPIDS

DOC. NO. CPI:

C2001-140502

TITLE:

New thdF polypeptides and polynucleotides obtained from Streptococcus pneumoniae, useful as research

reagents for discovering treatments of and

diagnostics for diseases, specifically those caused

by S. pneumoniae.

DERWENT CLASS:

B04 D16

INVENTOR(S):

BISWAS, S; HOLMES, D J; INGRAHAM, K A; SO, C Y; VAN

HORN, S; ZALACAIN, M

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC

COUNTRY COUNT:

20

PATENT INFORMATION:

PA	CENT	NO	KIND	DATE	WEEK	LA	PG
WO	2003	10533	34 A1	20010726	(200150)*	EN	39

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR W: JP

# APPLICATION DETAILS:

PATENT NO KIND	APPLICATION	DATE
WO 2001053334 A1	WO 2001-US1584	20010118

PRIORITY APPLN. INFO: US 2000-487514 20000119

AN 2001-465364 [50] WPIDS

AB WO 200153334 A UPAB: 20010905

NOVELTY - An isolated polypeptide comprising a sequence that is either at least 95% identical to, comprising, or having a fully defined 457 amino acid sequence (I) given in the specification, or is encoded by a recombinant polynucleotide comprising a fully defined 1374 bp sequence (II) also given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide comprising a sequence:

(a) encoding a polypeptide having at least 95% identity to the(I);

(b) having at least 95% identity over its entire length to a

polynucleotide encoding (I);

- (c) having at least 95% identity to (II);
- (d) that encodes (I);
- (e) that is (II);
- (f) of at least 30 nucleotides in length obtained by screening an appropriate library under stringent conditions with a probe having the sequence (II) or its fragment of at least 30 nucleotides;
- (g) encoding a mature polypeptide expressed by the thdF gene comprised in the Streptococcus pneumoniae; and
  - (h) a complement of (a)-(g);
  - (2) a method of treating an individual:
- (a) in need of enhanced activity or expression of or immunological response to (I) by administering an antagonist of (I); or
- (b) having the need to inhibit activity or expression of (I) by administering an antagonist of (I), a nuclei acid that inhibits the expression of a polynucleotide encoding (I), a polypeptide that competes with (I) for its ligand, substrate or receptor, or a polypeptide that induces an immunological response to the polypeptide in the individual;
- (3) a **process** for diagnosing or prognosing a disease or susceptibility to a disease related to expression or activity of (I) in an individual by:
- (a) determining the presence of a mutation in the nucleotide sequence encoding (I) in an organism in the individual; or
- (b) analyzing for the presence or amount of the polypeptide expression in a sample derived from the individual;
- (4) a process for producing (I) by culturing a host cell under conditions for the production of (I);
- (5) a **process** for producing a host cell comprising an expression system or a membrane expressing (I) by transforming or transfecting a cell with an expression system comprising a polynucleotide capable of producing (I) when the expression system is present in a compatible host cell such that the host cell produces the polypeptide;
  - (6) a host cell or a membrane expressing (I);
  - (7) an antibody immunospecific for (I);
- (8) a **method** for screening to identify compounds that agonize or inhibit the function of (I) by:
- (a) measuring the binding of a candidate compound to the polypeptide (or to the cells or membranes bearing the polypeptide) or a fusion protein by means of a label directly or indirectly associated with the candidate compound, or in the presence of a labeled competitor;
- (b) testing whether the candidate compound results in a signal generated by activation or inhibition of the polypeptide, using detection systems appropriate to the cells or cell membranes bearing the polypeptide;
- (c) mixing the candidate compound with a solution comprising(I) to form a mixture, measuring activity of the polypeptide in the mixture, and comparing the activity of a mixture to a standard; or
- (d) detecting the effect of a candidate compound on the production of mRNA encoding the polypeptide and the polypeptide in cells, using for instance, an ELISA assay; and
  - (9) an agonist or antagonist to the (I).

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Peptide therapy; gene therapy.

USE - The polynucleotides and polypeptides may be used as

research reagents and materials for the discovery of treatments of and diagnostics for diseases, particularly human diseases, in determining disease stage, course, the response of an infectious organism to drugs, determining the susceptibility to a disease. The polynucleotides and polypeptides are particularly useful for diagnosing bacterial infections, specifically infections caused by Streptococcus pneumoniae. These may further be used to for screening compounds that antagonize or agonize the functions of the polypeptides and polynucleotides, to configure screening methods for detecting the effect of added compounds on the production of mRNA and/or polypeptide in cells, to identify membrane bound or soluble receptors, and to prevent the adhesion of bacteria to eukaryotic, preferably mammalian, extracellular matrix protein on in-dwelling devices to extracellular matrix proteins in wounds, to block bacterial adhesion between eukaryotic extracellular matrix proteins and bacterial thdF proteins that mediate tissue damage, or to block normal progression of pathogenesis in infections initiated other than by implantation of in-dwelling devices or by other surgical techniques. The polynucleotides may be used as hybridization probes for RNA, cDNA and genomic DNA to isolate full length cDNAs and genomic clones encoding thdF, and to isolate cDNA and genomic clones of other genes that have a high identity, particularly high sequence identity to a thdF gene. Dwq.0/0

L22 ANSWER 11 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

2001-226696 [23] WPIDS

DOC. NO. CPI:

C2001-067684

TITLE:

New DnaE polypeptides of Streptococcus pneumoniae for diagnosing and treating microbial infections, especially infection by Streptococcus pneumoniae and Helicobacter pylori.

DERWENT CLASS:

B04 D16

INVENTOR(S):

MAY, E; VAN HORN, S; WARREN, P V; WARREN, R L (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC

COUNTRY COUNT:

20

PATENT INFORMATION:

PATENT ASSIGNEE(S):

PATENT	NO	KIND	DATE.	WEEK	LA	PG

WO 2001016351 A1 20010308 (200123) \* EN 43

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: JP

US 6280990 B1 20010828 (200151)

# APPLICATION DETAILS:

PATENT NO F	(IND	APPL	LICATION	DATE
WO 2001016351	A1 .	WO 2	2000-US22973	20000822
US 6280990	B1	US 1	L999-387695	19990831

PRIORITY APPLN. INFO: US 1999-387695 19990831

ΑN 2001-226696 [23] WPIDS

AB WO 200116351 A UPAB: 20010425

NOVELTY - An isolated DnaE polypeptide (I) of Streptococcus

pneumoniae comprising a sequence having at least 95 % identity to a sequence (S1) of 1042 amino acids, given in the specification, a sequence comprising S1, S1, or a sequence encoded by a recombinant polynucleotide comprising a sequence (S2) of 3129 nucleotides given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) an isolated polynucleotide (II) selected from a polynucleotide comprising a sequence encoding a polypeptide having at least 95 % identity to S1, a polynucleotide having at least 95 % identity to a sequence encoding S1, a polynucleotide comprising a sequence having at least 95 % identity to S2, a polynucleotide encoding S1, S2, a polynucleotide with a sequence of at least 30 nucleotides in length obtained by screening an appropriate library under stringent hybridization conditions with a probe having S1, or its fragment having at least 30 nucleotides in length, a polynucleotide encoding a mature polypeptide expressed by the dnaE gene comprised in S. pneumoniae, or a polynucleotide complementary to the above polynucleotides;
  - (2) treating an individual:
- (i) in need of enhanced activity or expression of or immunological response to (I) comprising administering an antagonist of (I); or
- (ii) having need to inhibit activity or expression of (I) comprising administering:
  - (a) an antagonist to (I);
- (b) a nucleic acid that inhibits the expression of a polynucleotide sequence encoding (I);
- (c) a polypeptide that competes with (I) for its ligand, substrate, or receptor; or
- (d) a polypeptide that induces an immunological response to (I) in the individual;
- (3) diagnosing or prognosing a disease or susceptibility to a disease in an individual related to the expression or activity of (I), comprising determining the presence or absence of a mutation in the nucleotide sequence encoding (I) in an organ of the individual, or analyzing for the presence or the amount of expression of (I) in a sample derived from the individual;
  - (4) producing (I) comprising culturing host cell;
- (5) producing a host cell or a membrane, comprising an expression system capable of expressing (I), by transforming or transfecting a cell with an expression system comprising a polynucleotide capable of producing (I) when the expression system is present in a compatible host cell, such that the host cell produces (I) under appropriate conditions;
- (6) a host cell or its membrane (III), capable of expressing
  (I);
  - (7) an antibody (Ab) immunospecific for (I);
- (8) screening to identify compounds which agonize or inhibit the function of (I), by:
- (a) measuring the binding of a candidate compound (CC) to (I),(III) or a fusion protein comprising (I), using a label, directly or indirectly associated with CC;
- (b) measuring the binding of CC to (I), (III) or a fusion protein comprising (I), in the presence of a labeled competitor;
- (c) testing whether CC results in signal generated by activation or inhibition of (I), using detection systems appropriate to (III);

(d) mixing CC with a solution containing (I) to form a mixture, measuring activity of (I) in the mixture, and comparing the activity of the mixture to a standard; or

(e) detecting the effect of CC on the production of mRNA encoding (I), and (I) in cells, using for instance, an enzyme linked immunosorbant assay (ELISA); and

(9) an agonist or antagonist of (I).

ACTIVITY - Antimicrobial; cytostatic; antiulcer; antiinflammatory.

MECHANISM OF ACTION - Gene therapy; vaccine. No biological data is given.

USE - An antagonist of (I) is useful for treating an individual in need of enhanced activity or expression of or immunological response to (I). An antagonist of (I), a nucleic acid molecule that inhibits expression of a nucleic acid (II) encoding (I), a polypeptide that competes with (I) for its ligand, substrate or receptor, and a polypeptide that induces an immunological response to (I) are useful for inhibiting activity or expression of (I) (claimed). (I) and (II) are useful for treating and diagnosing microbial infections such as infection caused by S. pneumoniae and Helicobacter pylori. (I) and (II) are useful for treating diseases such as H. pylori-induced cancers, e.g. gastrointestinal carcinoma, gastric ulcers, and gastritis. Dwg.0/0

WPIDS (C) 2002 THOMSON DERWENT L22 ANSWER 12 OF 49

ACCESSION NUMBER:

2001-016077 [02]

DOC. NO. CPI:

C2001-004433

TITLE:

Novel 5-enolpyruvylshikimate-3-phosphate synthase protein from Streptococcus pneumoniae useful for identifying agonists and antagonists of aroA

activity for treating otitis media, conjunctivitis

and pneumonia.

DERWENT CLASS:

B04 D16

INVENTOR(S):

BROWN, J R; CHALKER, A F; DU, W; KATZ, L K;

WPIDS

MAZZULLA, M J; PAYNE, D J; TRAINI, C M

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC

COUNTRY COUNT:

27

PATENT INFORMATION:

PATENT	NO	KIND	DATE	WEEK	LA	PG

WO 2000068243 A1 20001116 (200102)\* EN 70

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: JP US

EP 1179002 A1 20020213 (200219) EN

> R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

# APPLICATION DETAILS:

111111111111111111111111111111111111111	IND		PLICATION	DATE
WO 2000068243	A1	WO	2000-US12251	20000504
EP 1179002	A1	ΕP	2000-928848	20000504

Shears 308-4994 Searcher :

WO 2000-US12251 20000504

## FILING DETAILS:

PRIORITY APPLN. INFO: US 1999-133070P 19990507

AN 2001-016077 [02] WPIDS

AB WO 200068243 A UPAB: 20010110

NOVELTY - A polypeptide (I) comprising 70 % identity to a 427 residue amino acid sequence (S2), fully defined in the specification, and corresponding to 5-enolpyruvylshikimate-3-phosphate synthase (AroA) from Streptococcus pneumoniae, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for

the following:

- (1) an isolated polynucleotide (II) comprising 70 % identity to a polynucleotide encoding a polypeptide comprising (S2), or to a polynucleotide encoding the same mature polypeptide expressed by the aroA gene contained in the S. pneumoniae of the deposited strain, or comprising a sequence encoding (I), a sequence complementary to the above mentioned polynucleotides, or a sequence which comprises at least 15 sequential bases of the above mentioned polynucleotides;
  - (2) a vector (III) comprising (II);
  - (3) a host cell (IV) comprising (III);
- (4) preparation of (I), comprising culturing (IV) under optimum conditions sufficient for the production of the polypeptide or its fragment;
  - (5) an antibody (V) against (I);
- (6) identifying compounds which interact with and inhibit or activate an activity of (I), comprising:
- (a) contacting a composition comprising the polypeptide with the compound to be screened under interaction conditions, the interaction being associated with a second component capable of providing detectable signal in response to the interaction of the polypeptide with the compound; and
- (b) determining if the compound interacts with and activates or inhibits an activity of the polypeptide by detecting the presence or absence of a signal generated from the interaction of the compound with the polypeptide;
- (7) an antagonist (VI) which inhibits the activity or expression of (I);
- (8) an antagonist that inhibits, or an agonist (VII) that activates, an activity of the polypeptide which comprises 90 % identity to (S2) or a 415 residue amino acid sequence (S4), fully defined in the specification, the activity of the protein being:
  - (a) synthesis of p-aminobenzoate and ubiquinone;
- (b) transformation of phospho(enol)pyruvate (PEP) and shikimate 3-phosphate (S3P) to 5-enolpyruvylshikimate-3-phosphate synthase (EPSP) an inorganic phosphate (Pi);
  - (c) transformation of EPSP and Pi to PEP and S3P;
- (d) binding of
  - (i) AroA and PEP;
  - (ii) AroA to PEP-pyruvate kinase complex;
  - (iii) AroA to PEP-lactate dehydrogenase complex; and
  - (iv) AroA and S3P;
  - (e) competitive inhibition of the forward reaction of AroA by

- (i) glyphosate versus PEP (ii) EPSP versus PEP and (iii) EPSP versus S3P;
- (f) competitive inhibition of the reverse reaction of AroA by S3P versus EPSP;
- (g) uncompetitive inhibition of the forward reaction of AroA by glyphosate versus S3P;
- (h) uncompetitive inhibition of the reverse reaction of AroA by(i) glyphosate versus EPSP and (ii) S3P versus Pi; and
- (i) noncompetitive inhibition of the reverse reaction of AroA by glyphosate versus Pi;
- (9) treating an individual infected with bacteria by administering a compound that is a competitive inhibitor of S3P substrate use by AroA;
- (10) inhibiting an activity of AroA, and a conversion of acetyl-CoA to a product or conversion of malonyl-ACP to product, comprising contacting a composition comprising bacteria with a compound that inhibits the activity for a sufficient time to cause killing or slowing growth of the bacteria; and
  - (11) inhibiting growth of bacteria.

ACTIVITY - Antibacterial; antiinflammatory; ophthalmological. No biological data is given.

MECHANISM OF ACTION - AroA activity inhibitors; immune response stimulator; bacterial adherence to damaged tissues, inhibitor; gene therapy.

USE - (I) is useful for treating an individual in need of AroA polypeptide. (I) and (II) are useful as diagnostic reagents for diagnosing a disease related to their expression or activity in an individual which comprises determining a nucleic acid sequence encoding the polypeptide and/or analyzing for the presence or amount of the polypeptide in a sample derived from the individual. (I) is useful for inducing an immunological response in a mammal comprising inoculating the polypeptide, its fragment or variant, or delivering a nucleic acid vector to direct expression of the polypeptide in vivo, in order to induce an immunological response to produce antibody and/or T-cell immune response to protect the animal from the disease. (VI) is useful for inhibiting the activity of the AroA polypeptide and for inhibiting the growth of a bacterial composition and also for inhibiting AroA polypeptide. (VII) is used to inhibit or activate AroA polypeptide and for treating individuals infected with bacteria of the genus Staphylococcus, S. aureus, a member of Streptococcus genus such as Streptococcus pneumoniae. (All claimed). (I), its antagonists and agonists are useful for treating otitis media, conjunctivitis, pneumonia, bacteremia, meningitis, sinusitis, pleural empyema and endocarditis and most particularly meningitis. (II) is useful for gene therapy techniques. The polynucleotides may be used as hybridization probes to isolate full length cDNAs and genomic clones encoding AroA and to isolate cDNA and genomic clones of other genes that have a high sequence similarity to the AroA gene. (I) and (II) are also useful as research reagents and materials for discovery of treatments of and diagnostics for human diseases. The DNA sequences may be used in the discovery of antibacterial compounds and to construct antisense sequences to control the expression of the coding sequence of interest. The encoded protein is useful as a target for screening antibacterial drugs. The polynucleotides or its fragments which encode non-variable regions of the bacteria cell surface proteins in DNA constructs used in the genetic immunization experiments in animal models of Streptococcus pneumoniae infections are useful in

identifying protein epitopes able to provoke a prophylactic or therapeutic immune response. The polypeptides are used as antigens for vaccination of a host to produce specific antibodies which protect against invasion of bacteria by blocking adherence of bacteria to damaged tissues such as wounds in the skin or connective tissue caused by mechanical, chemical or thermal damage, or by implantation of indwelling devices, or wounds in the mucous membranes. The novel molecules are useful for preventing adhesion of gram positive and/or gram negative bacteria, to mammalian extracellular matrix proteins on in-dwelling devices or to extracellular matrix proteins in wounds, to block AroA protein-mediated cell invasion by initiating phosphorylation of mammalian tyrosine kinases, to block bacterial adhesion between mammalian extracellular matrix proteins and bacterial AroA proteins that mediate tissue damage and/or to block the normal progression of pathogenesis in infections initiated other than by the implantation of in-dwelling devices or by other surgical techniques. Dwg.0/6

L22 ANSWER 13 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2000-68

2000-687653 [67] WPIDS

DOC. NO. CPI:

C2000-209393

TITLE:

Streptococcus pneumoniae yphC protein and DNA

sequence, useful for treating infections,

meningitis, and bacteremia.

DERWENT CLASS:

B04 D16

INVENTOR(S):

BISWAS, S; BURNHAM, M K R; CHALKER, A F; HOLMES, D J; INGRAHAM, K A; SO, C Y; TRAINI, C M; VAN HORN,

S; WARREN, P V; WARREN, R L; ZALACAIN, M

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC

COUNTRY COUNT:

19

PATENT INFORMATION:

 	10 K	 	WEEK	 PG
 			(200067)*	39

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE W: JP

# APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 20000684	27 A1	WO 2000-US11894	20000502

PRIORITY APPLN. INFO: US 1999-307003 19990507

AN 2000-687653 [67] WPIDS

AB WO 200068427 A UPAB: 20001223

NOVELTY - A novel isolated polypeptide (A) comprising the 436 residue Streptococcus pneumoniae yphC (GTP binding proteins) family protein given in the specification.

DETAILED DESCRIPTION - A novel isolated polypeptide (A), yphC, comprises:

(1) an isolated polypeptide comprising an amino acid (aa) sequence having at least 95% identity to aa sequence (I) of 436 aa from Streptococcus pneumoniae given in the specification, over the

entire length of (I);

- (2) an isolated polypeptide comprising (I);
  - (3) an isolated polypeptide which is (I); or
- (4) a polypeptide which is encoded by a recombinant polynucleotide comprising polynucleotide sequence (II) of 1311 base pairs (bp) given in the specification.

INDEPENDENT CLAIMS are also included for the following:

- (1) an isolated polynucleotide selected from:
- (i) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide with at least 95% identity to (I), over the entire length of (I);
- (ii) an isolated polynucleotide comprising a polynucleotide sequence that has at least 95% identity over its entire length to a polynucleotide sequence encoding (I);
- (iii) an isolated polynucleotide comprising a nucleotide sequence that has at least 95% identity to (II), over the entire length of (II);
- (iv) an isolated polynucleotide comprising a nucleotide
  sequence encoding (I);
  - (v) an isolated polynucleotide which is (II);
- (vi) an isolated polypeptide at least 30 nucleotides long, obtained by screening an appropriate library under stringent hybridization conditions with a probe having the sequence of (II), or a fragment of (II) at least 30 nucleotides long;
- (vii) an isolated polynucleotide encoding a mature polypeptide expressed by the yphC gene contained in Streptococcus pneumoniae; and
- (viii) a polynucleotide complementary to the isolated polynucleotide of (i)-(vii);
  - (2) a method for the treatment of an individual:
- (a) in need of enhanced activity or expression of or immunological response to (A), comprising administering to the individual an antagonist to (A); or
- (b) in need of inhibition of activity or expression of (A), comprising administering an antagonist to the polypeptide, a nucleic acid molecule that inhibits the expression of a polynucleotide sequence encoding (A), a polypeptide that competes with the (A) for its ligand, substrate, or receptor, or a polypeptide that induces an immunological response to (A) in the individual;
- (3) a process for diagnosing or prognosing a disease or a susceptibility to a disease in an individual related to expression of (A) in an individual, comprising determining the presence or absence of a mutation in the nucleotide sequence encoding (A) in an organism of the individual; or analyzing for the presence or amount of expression of (A) in a sample derived from the individual;
- (4) a **process** for producing (A), comprising culturing a host cell under conditions sufficient for the production of the polypeptide;
- (5) a process for producing a host cell comprising an expression system or a membrane expressing (A), comprising transforming or transfecting a cell with an expression system comprising a polynucleotide capable of producing (A) when the expression system is present in a compatible host cell, such that the host cell under culture conditions produces the polypeptide;
  - (6) a host cell or a membrane expressing (A);
  - (7) an antibody antigenic to or immunospecific for (A);
  - (8) a method for screening to identify compounds that

activate or inhibit the function of (A), comprising a method selected from:

- (a) measuring the binding of a candidate compound to (A) or to the cells or membranes bearing (A) or a fusion protein of it, by means of a label directly or indirectly associated with the candidate compound;
- (b) measuring the binding of a candidate compound to (A) or to the cells or membranes bearing (A) or a fusion protein of it in the presence of a labeled competitor;
- (c) testing whether the candidate compound results in a signal generated by activation or inhibition of (A), using detection systems appropriate to the cells or cell membranes bearing (A);
- (d) mixing a candidate compound with a solution with a solution containing (A) to form a mixture, measuring activity of (A) in the mixture, and comparing the activity of the mixture to a standard; or
- (e) detecting the effect of a candidate compound on the production of mRNA encoding (A) in cells, using e.g. an enzyme linked immunosorbent assay (ELISA) assay; and
  - (9) an agonist or antagonist to (A).

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - None given.

USE - The DNA sequence can be used to transform a host cell to produce the protein (claimed). The products can be used to treat bacterial infections (especially Streptococcus pneumoniae infections, and Helicobacter pylori infections), otitis media, conjunctivitis, pneumoniae, bacteremia, meningitis, sinusitis, pleural empyema, and endocarditis. Dwq.0/0

L22 ANSWER 14 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

2000-687324 [67]

DOC. NO. CPI:

C2000-209213

TITLE:

Novel isolated YycG polypeptide of Streptococcus

pneumoniae and polynucleotides encoding

WPIDS

polypeptides useful as diagnostic reagent for diagnosing a disease related to expression or

activity of polypeptide.

DERWENT CLASS:

B04 D16

INVENTOR(S):

BISWAS, S; BRYANT, A; BURNHAM, M K R; CHALKER, A F; HOLMES, D J; INGRAHAM, K A; SO, C Y; THROUP, J P;

VAN HORN, S; WARREN, R L; ZALACAIN, M

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC

COUNTRY COUNT:

19

PATENT INFORMATION:

KIND DATE PATENT NO WEEK LA

WO 2000065026 A2 20001102 (200067) \* EN

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: JP

APPLICATION DETAILS:

PATENT NO KIND APPLICATION WO 2000-US10991 20000424 WO 2000065026 A2

PRIORITY APPLN. INFO: US 1999-300489 19990428

AN 2000-687324 [67] WPIDS

AB WO 200065026 A UPAB: 20001223

NOVELTY - An isolated YycG polypeptide of Streptococcus pneumoniae (I) having a 449 residue amino acid sequence (S2), fully defined in the specification, is new.

DETAILED DESCRIPTION - An isolated YycG polypeptide of Streptococcus pneumoniae (I) having a 449 residue amino acid sequence (S2), fully defined in the specification, is new. (I) is an isolated polypeptide comprising a polypeptide sequence having 95 % identity to (S2) over its entire length, an isolated polypeptide comprising (S2), an isolated polypeptide that is (S2), or is a polypeptide encoded by the recombinant polynucleotide comprising a 1350 nucleotide sequence (S1), fully defined in the specification.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide (II) comprising:

- (a) a polynucleotide sequence encoding a polypeptide having 95 % identity to (S2) over its entire length;
- (b) a polynucleotide sequence encoding (S2) having 95 % identity over its entire length to a polynucleotide sequence encoding (S2),
- (c) a nucleotide sequence that has 95% identity to (S1) over its entire length, an isolated polynucleotide sequence comprising a nucleotide sequence encoding (S2);
  - (d) a nucleotide sequence which is (S1);
- (e) a sequence at least 30 nucleotides in length obtained by screening an appropriate library under stringent hybridization conditions with a labeled probe having the sequence of (S1), or its fragment having 30 nucleotides;
- (f) a sequence encoding a mature polypeptide expressed by the YycG gene comprised in S. pneumoniae; or
  - (g) the complement of any of (a)-(f);
  - (2) preparation of (I);
- (3) a process for producing a host cell comprising an expression system or its membrane expressing (I), comprising transforming or transfecting a cell with an expression system comprising (II) so that when the expression system is present in a host cell, the host cell produces (I), under appropriate culture conditions;
  - (4) a host cell (III) or its membrane expressing (I);
  - (5) an antibody (IV) immunospecific to (I);
- (6) screening to identify compounds that agonize or inhibit the function of (I), comprising:
- (a) measuring the binding of a candidate compound to the polypeptide, cells or membranes bearing the polypeptide, or a fusion protein, by means of a label directly or indirectly associated with the candidate compound;
- (b) measuring the binding of a candidate compound to the polypeptide or a fusion protein in the presence of a labeled competitor;
- (c) testing if the candidate compound results in a signal generated by activation or inhibition of the polypeptide using detection systems appropriate to the cells or cell membranes bearing the polypeptide, mixing the candidate compound with the solution containing (I) to form a mixture;
- (d) measuring the activity of the polypeptide in the mixture and comparing the activity of the mixture to a standard; or

(e) detecting the effect of a candidate compound on the production of mRNA encoding the polypeptide and the polypeptide in the cells by enzyme linked immunosorbent assay (ELISA); and (7) agonists or antagonists (V) of (I). ACTIVITY - Antibacterial; cytostatic; antiinflammatory; antiulcer. No biological data is given. MECHANISM OF ACTION - Initial physical attraction between the pathogen and mammalian extracellular protein, blocker; gene therapy. USE - (II) is useful as a diagnostic reagent for diagnosing a disease or a susceptibility to a disease in a subject related to expression or activity of (I) in a subject. The method comprises determining the presence or absence of a mutation in the nucleotide sequence encoding the polypeptide in the genome of a subject and/or analyzing for the presence or amount of the polypeptide expression in sample derived from the subject. (V) is used for treating a subject in need of enhanced activity or expression (I) or treating subjects having need to inhibit activity or expression of (I). (All claimed). The polypeptides may also be used to identify membrane bound or soluble receptors. Polynucleotides are also useful as hybridization probes for cDNA and genomic DNA, or as primers for a nucleic acid amplification reaction, to isolate full length cDNAs and genomic clones encoding (I) and to isolate cDNA and genomic clones of other genes. The polypeptides can also be used in the structure-based design of an agonist, antagonist or inhibitor of the polypeptide. The novel polypeptides and polynucleotides are useful as research reagents and materials for discovery of treatments and diagnosis of human diseases. (II) is also used for diagnosing a bacterial infection, caused by S. pneumoniae in a biological sample derived from an individual. YycG polypeptide overexpression can be used to detect the presence of infection in tissue samples from diseased individuals on comparison to normal tissue samples. The novel polypeptides and polynucleotides are useful for treating abnormal conditions such as a disease, related to either an excess of, an under expression of, elevated activity of, or decreased activity of YycG polypeptide and/or polynucleotide. The polynucleotide sequences can also be used in the discovery and development of antibacterial compounds. The novel polypeptides, polynucleotides, agonist or antagonist are useful in interfering with the initial physical attraction between a pathogen and a mammalian host which is responsible for further infection. The novel molecules are useful for preventing adhesion of gram positive and/or gram negative bacteria, to mammalian extracellular matrix proteins on in-dwelling devices or to extracellular matrix proteins in wounds, to block bacterial adhesion between eukaryotic, preferably mammalian, extracellular matrix proteins and bacterial YycG proteins that mediate tissue damage and/or to block the normal progression of pathogenesis in infections initiated other than by the implantation of in-dwelling devices or by other surgical techniques. The antimicrobial compounds (agonists and antagonists of YycG polypeptides and/or

Helicobacter pylori infection such as H. pylori induced cancers,

gastric ulcers and gastritis. The agonist and **antagonist** are employed as bacteriostatic or bactericidal agonist and

polynucleotides) are useful in the treatment of

antagonist, to prevent, inhibit and/or treat diseases. Dwg.0/0

L22 ANSWER 15 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

2000-679497 [66] WPIDS

DOC. NO. CPI:

C2000-206646

TITLE:

Novel polypeptide and polynucleotide of gyrase family useful for diagnosis and treatment of

microbial diseases and for identifying

antibacterial compounds.

DERWENT CLASS:

B04 D16

INVENTOR(S):

WARREN, R L; WILDING, E I

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC

COUNTRY COUNT:

20

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2000061787 A2 20001019 (200066) \* EN 58

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: JP

US 6346397 B1 20020212 (200219)

## APPLICATION DETAILS:

PATENT NO KIND	APPLICATION	DATE
WO 2000061787 A2 US 6346397 B1 Provisional	WO 2000-US9661 US 1999-128991P US 2000-546990	20000412 19990412 20000411

PRIORITY APPLN. INFO: US 1999-128991P 19990412; US 2000-546990 20000411

AN 2000-679497 [66] WPIDS

AB WO 200061787 A UPAB: 20001219

NOVELTY - An isolated gyrA (a member of Gyrase family) polypeptide (I) of Streptococcus pneumoniae, comprising a sequence having at least 70 %, 80 %, 90 % or 95 % identity to an 841 residue amino acid sequence, fully defined in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) an isolated polynucleotide (II) encoding (I), comprising a nucleotide sequence that has at least 70 %, 80 %, 90 % or 95 % identity to a 5449 base pair sequence, fully defined in the specification, or its complement or a polynucleotide obtained by screening a library under stringent hybridization conditions with a labeled probe having the sequence of (II) or its fragment;
- (2) an expression system (III) comprising (II) present in a compatible host cell;
- (3) producing a recombinant host cell by transforming a cell with (III), so that the host cell produces (I);
- (4) a recombinant host cell ( $\overline{IV}$ ) comprising ( $\overline{III}$ ), or produced by the **method** of (3), or its membrane expressing ( $\overline{II}$ );
- (5) preparation of (I), comprising culturing (IV) under expression conditions and recovering the polypeptide;

- (6) an antibody immunospecific for (I);
- (7) an agonist or antagonist to (I);
- (8) a computer readable medium having stored (I) or (II), a data set representing (I) or (II); and
- (9) a computer based method for performing homology identification, comprising providing (II) in a computer readable medium and comparing the polynucleotide sequence to at least one polynucleotide or polypeptide sequence to identify homology.

ACTIVITY - Antibiotic; Antiinflammatory; Auditory; Antiulcer.

No biological data is given.

MECHANISM OF ACTION - Vaccine; gene therapy.

USE - Agonists or antagonists to (I) or nucleic acid molecules that enhance or inhibit the expression of (II), are useful for treating an individual in need of enhanced activity or to inhibit the expression of (I). (I) and (II) are useful for diagnosing a disease or a susceptibility to a disease in an individual by determining the presence or absence of a mutation in the nucleotide sequence encoding (I) in the genome of the individual, or by analyzing for the presence of expression of (I) in a sample derived from the individual. (I) is also useful for screening compounds which inhibit or stimulate the function of (I) by using a label directly or indirectly associated with the compound. Alternatively, the screening methods involve competition with a labeled competitor. These screening methods may test if the compound results in a signal generated by activation or inhibition of the polypeptide, using a detection system appropriate to the cells bearing the polypeptide. Further the screening methods comprise mixing a candidate compound with a solution comprising the polypeptide, and measuring the activity of the polypeptide in the mixture and comparing the activity to a standard, or by detecting the effect of the compound on the production of mRNA encoding the polypeptide by enzyme linked immunosorbent assay (ELISA). A composition comprising the polypeptide is contacted with the compound to be screened under conditions to permit interaction between them, and the interaction is associated with a second component capable of providing a detectable signal which is determined (all claimed). (II) may be used as a hybridization probe for RNA, cDNA and genomic DNA to isolate full-length cDNAs and genomic clones encoding (I). (I) is useful as an immunogen to produce antibodies immunospecific for the polypeptides. (I) and (II) are useful as vaccines for inducing an immunological response in a mammal, to protect against bacterial infections, in particular Streptococcus pneumoniae infection, and for preventing adhesion of bacteria to extracellular matrix proteins on in-dwelling devices or to extracellular matrix proteins in wounds. The antagonists and agonists identified using (I) are useful in the prevention, or treatment of Helicobacter pylori infection such as gastrointestinal carcinoma, gastric ulcer and gastritis. (I) and (II) are useful as components in databases useful for search analysis as well as in sequence analysis algorithms. Diseases treated include infection by a bacteria, for example otitis media, conjunctivitis, pneumonia, bacteremia, meningitis, sinusitis, pleural empyema, endocarditis and particularly meningitis. Dwg.0/0

L22 ANSWER 16 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2000-548599 [50] WPIDS

DOC. NO. NON-CPI: N2000-405865 DOC. NO. CPI: C2000-163688

TITLE: Streptococcus pneumoniae fabZ proteins useful for

diagnosing and treating microbial infections.

DERWENT CLASS: B04 D16 S03 T01

INVENTOR(S): KONSTANTINIDIS, A K; RUSSELL, R B; WARREN, P V;

KONSTANTINIDIS, A

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC

COUNTRY COUNT: 20

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2000030662 A1 20000602 (200050)\* EN 51

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: JP

US 6277595 B1 20010821 (200150)

#### APPLICATION DETAILS:

		NO I	KIND		PLICATION	DATE
		030662			1999-US26435	
US	6277	595	B1	US	1998-196388	19981119

PRIORITY APPLN. INFO: US 1998-196388 19981119

AN 2000-548599 [50] WPIDS

AB WO 200030662 A UPAB: 20001010

NOVELTY - Nucleic acids (I) encoding a polypeptide (II) designated fabZ, a member of the fatty acid biosynthetic pathway family of proteins from Streptococcus pneumoniae.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

- (1) an isolated polynucleotide (I), comprising either:
- (a) a polynucleotide comprising a sequence encoding a polypeptide that has 70-95% identity with a fully defined 140 amino acid sequence (IIa) (given in the specification);
- (b) a polynucleotide comprising a sequence that has 70-95% identity to a polynucleotide sequence encoding (IIa) over its entire length;
- (c) a isolated polynucleotide comprising a sequence that has 70-95% identity to a defined 423 nucleotide sequence (Ia) given in the specification;
  - (d) a polynucleotide which encodes (IIa)
  - (e) a polynucleotide comprising (Ia);
- (f) a polynucleotide obtained by screening a library under stringent conditions with a probe comprising (Ia);
- (g) an isolated polynucleotide sequence encoding a mature fabZ protein of S. pneumoniae; and/or
  - (h) a sequence complementary to (a)-(g);
  - (2) a polypeptide selected from:
- (a) a peptide comprising an amino acid sequence having 70-95% identity to (IIa) over its entire length;
  - (b) a peptide comprising (IIa);

- (c) a peptide that is (IIa); and/or
- (d) a polypeptide encoded by a recombinant polynucleotide comprising (Ia);
  - (3) an antibody (III) antigenic for (Ia);
  - (4) a method (IV) for the treatment of an individual:
- (a) in need of enhanced activity or expression of (II), comprising:
  - (i) administering an agonist of (II); and/or
- (ii) providing the individual with (II) to produce the polypeptide (and its activity) in vivo; or
  - (b) in need of inhibited activity of (II), comprising:
  - (i) administering an antagonist of (II); and/or
- (ii) administering a nucleic acid molecule that inhibits the expression of (I); and/or
- (iii) administering a polypeptide that competes with the polypeptide for its ligand, substrate or receptor;
- (5) a method (V) for diagnosing or prognosing a disease or a susceptibility to a disease in an individual related to expression or activity of (II), comprising:
- (a) determining the presence or absence of a mutation in the sequence (IIa) in the genome of the individual; and/or
- (b) analyzing and quantifying the presence of the polypeptide(II) in a sample from the individual;
- (6) a method (VI) for screening to identify compounds that activate or inhibit the function of (II), comprising:
- (a) measuring the binding of a candidate compound (CC) to (II) or to cells or membranes bearing (II) (of a fusion protein of (II)) using a label directly or indirectly associated with the CC;
- (b) measuring the binding of a CC to (II) or to cells or membranes bearing (II) (of a fusion protein of (II)) in the presence of a labeled competitor;
- (c) testing whether a CC results in a signal generated by activation or inhibition of (II), using detection systems appropriate to the cells or membranes bearing (II);
- (d) mixing a CC with a solution containing (II) and measuring the activity of the polypeptide in the mixture, and comparing that activity to a standard;
- (e) detecting the effect of a CC on the production of mRNA encoding (II) and (II) in cells using, for example, an enzyme linked immunosorbant assay; and/or
  - (f) a method comprising:
- (i) contacting (II) with the CC and assessing their interactions; and
- (ii) determining whether the compound interacts with and activates or inhibits the activity of (II) by detecting the presence of absence of a signal generated from the interaction of the compound and polypeptide);
  - (7) an (ant)agonist (VII) of the expression or activity of (I);
- (8) an expression system (VIII) comprising the polynucleotide(I) and capable of expressing (II) when present in a host cell;
- (9) a host cell (IX) comprising (VIII) or a membrane expressing
  (II);
- (10) a process (X) for producing a polypeptide comprising
  culturing (IX);
- (11) a process (XI) for producing (IX) or a membrane of (IX) expressing (II), comprising transforming/transfecting a cell with (VIII), so that the cell expresses (II);
  - (12) a computer readable medium (XII), upon which is stored:

- (a) (Ia) or sequence(s) comprising (Ia) (and/or other polynucleotide sequences);
- (b) (IIa) or sequence(s) comprising (IIa) (and/or other polypeptide sequences);
  - (c) a data set representing (Ia);
  - (d) a data set representing polynucleotides encoding (IIa);
- (13) a computer based method (XIII) for performing homology identification, comprising providing a sequence comprising (Ia) in a computer readable medium and comparing that sequence to other polypeptides and polynucleotide to identify sequence homology;
- (14) a computerized method (XIV) for polynucleotide assembly, comprising providing a nucleic acid comprising (Ia) in a computer readable medium and screening for at least 1 overlapping region between that polynucleotide sequence and a second polynucleotide sequence; and
  - (15) a polynucleotide (XV) of the formula:
  - 5' X-(R1)m-(R2)-(R3)n-Y 3'
- X = H, a metal or a modified nucleotide residue or together with Y defines a covalent bond;
- Y = H, a metal or a modified nucleotide residue or together with X defines a covalent bond;
- R1 and R3 = any nucleic acid residue or modified nucleic acid residue;

R2 = the nucleotide sequence (Ia); and

m and n = 0-3000.

ACTIVITY - Bactericide.

MECHANISM OF ACTION - Vaccine.

No data given.

- USE (I) and (II) may be used in the prevention, treatment and diagnosis of diseases associated with fabZ expression and Streptococcal infection.
- (I) or (II) may be administered to treat diseases by rectifying mutations or deletions in a genome that affect the activity of fabZ by expressing inactive proteins or to supplement the production of fabZ polypeptides. Additionally, (I) may be used to produce fabZ, according to standard recombinant DNA methodology, by inserting the nucleic acids into a host cell and culturing the cell to express the protein (either in vitro or in vivo). Antisense nucleic acid molecules may be administered to down regulate fabZ expression by binding with the cells own fabZ genes and preventing their expression.
- (I) and complementary sequences may be used as probes in diagnostic assays to detect the presence of fabZ in samples.

The polypeptides may be used as antigens in the production of antibodies against fabZ and in assays to identify modulators of fabZ expression and activity. The anti-fabZ antibodies and fabZ antagonists may also be used to down regulate fabZ expression and activity. They may be used to treat S. pneumoniae infections.

The anti-fabZ antibodies may also be used as diagnostic agents for detecting the presence of fabZ polypeptides in samples.  ${\tt Dwg.0/0}$ 

L22 ANSWER 17 OF 49

WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

2000-533181 [48] WPIDS

DOC. NO. CPI:

C2000-158916

TITLE:

Nucleic acids encoding thymidylate kinase family polypeptides derived from Streptococcus pneumoniae, useful for screening for antibacterial agents.

DERWENT CLASS:

B04 D16

INVENTOR(S):

BISWAS, S; BURNHAM, M K R; CHALKER, A F; INGRAHAM,

K A; TRAINI, C M; WARREN, P V; ZALACAIN, M

PATENT ASSIGNEE(S):

(BISW-I) BISWAS S; (BURN-I) BURNHAM M K R; (CHAL-I) CHALKER A F; (INGR-I) INGRAHAM K A; (TRAI-I) TRAINI

C M; (WARR-I) WARREN P V; (ZALA-I) ZALACAIN M;

(SMIK) SMITHKLINE BEECHAM CORP

COUNTRY COUNT:

20

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2000050602 A1 20000831 (200048)\* EN 37

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: JP

US 6270762

B1 20010807 (200147)

US 2001027183 A1 20011004 (200161)

# APPLICATION DETAILS:

PATENT NO KIND	APPLICATION	DATE
WO 2000050602 A1 US 6270762 B1 US 2001027183 A1 Div ex	WO 2000-US4238 US 1999-259109 US 1999-259109 US 2000-749972	20000218 19990226 19990226 20001228

PRIORITY APPLN. INFO: US 1999-259109 19990226; US 2000-749972 20001228

AN 2000-533181 [48] WPIDS

AB WO 200050602 A UPAB: 20001102

NOVELTY - Nucleic acids (II) encoding polypeptides (I) of the thymidylate kinase family (tdk polypeptides) derived from Streptococcus pneumoniae, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

- (1) an isolated polypeptide (I), comprising:
- (a) an isolated amino acid sequence with at least 95% identity to a 210 residue amino acid (aa) sequence given in the specification (A1) over its entire length;
  - (b) an isolated polypeptide that is or comprises (A1);
- (c) a polypeptide encoded by a recombinant polynucleotide comprising a 637 base pair (bp) polynucleotide sequence given in the specification (N1);
  - (2) an isolated polynucleotide (II), comprising:
- (a) an isolated polynucleotide comprising a sequence encoding a polypeptide that has at least 95% identity to the amino acid sequence (A1) over its entire length;
- (b) an isolated polynucleotide comprising a sequence that has at least 95% identity over its entire length to a polynucleotide sequence encoding (A1);
- (c) an isolated polynucleotide comprising a sequence that has 95% identity to (N1) over its entire length;
- (d) an isolated polynucleotide comprising a sequence encoding
  (A1);
  - (e) an isolated polynucleotide that is (N1);
  - (f) an isolated polynucleotide at least 30 nucleotides in

length obtainable by screening an appropriate library under stringent conditions with a probe comprising (N1) or a 30 nucleotide fragment of (N1);

- (g) an isolated polynucleotide encoding a mature polypeptide expressed by the tdk gene in Streptococcus pneumoniae; and
  - (h) a polynucleotide sequence complimentary to (a)-(g);
  - (3) a method (III) for the treatment of a patient:
- (a) in need of enhanced activity or expression of or immunological response to (I), comprising administering an antagonist of the polypeptide; or
- (b) in need of inhibited expression or activity of (I), comprising:
  - (i) administering an antagonist to (I);
- (ii) administering a nucleic acid molecule that inhibits the expression of a polynucleotide sequence encoding (I);
- (iii) administering a polypeptide that competes with (I) for its ligand, substrate or receptor; and/or
- (iv) administering a polypeptide that induces an immunological
  response to (I) in the patient;
- (4) a **process** (IV) for diagnosing or prognosing a disease or susceptibility to a disease related to the expression and/or activity of (I) in a patient, comprising:
- (a) determining the presence or absence of a mutation in the nucleotide sequence encoding (I) in an organism in the patient; or
- (b) analyzing for the presence or amount of polypeptide expression in a sample from the patient;
- (5) a **process** (V) for producing (I) comprising culturing a host cell under conditions suitable for production of the polypeptide;
- (6) a process (VI) for producing a host cell containing an expression system or membrane expressing (I), comprising transforming or transfecting the cell with an expression system comprising a polynucleotide encoding (I), so that when in the host cell and under suitable conditions, the polynucleotide produces (I);
  - (7) a host cell (VII) or membrane expressing (I);
  - (8) an antibody (VIII) immunospecific for (I);
- (9) a method (IX) of screening to identify compounds that antagonize or inhibit the function of (I), comprising:
- (a) measuring the binding of a candidate compound to (I) (or cells and membranes bearing (I)) or a fusion protein of (I) using a label directly or indirectly associated with the candidate compound;
- (b) measuring the binding of a candidate compound to (I) (or cells and membranes bearing (I)) or a fusion protein of (I) in the presence of a labeled competitor;
- (c) testing whether the candidate compound results in a signal generated by activation or inhibition of (I), using detection systems appropriate to the cells or membranes bearing (I);
- (d) mixing a candidate compound with a solution comprising (I) to form a mixture, measuring activity of the peptide in the mixture and comparing the activity of the mixture to a standard; and/or
- (e) detecting the effect of a candidate compound on the production of mRNA encoding (I), using for example an ELISA (enzyme linked immunosorbant assay) test; and
  - (10) an agonist (X) or antagonist (XI) of (I).
- ACTIVITY None given for the tdk peptide per se. However, antagonists of (I) are antimicrobial.

MECHANISM OF ACTION - Thymidylate kinase enzyme.

No biological data given.

USE - The nucleic acids (II) may be used to recombinantly produce the tdk polypeptides either in vivo (e.g. as part of a genetic vaccination procedure) or in vitro (e.g. as part of a fermentation culture) (i.e. (V)). The nucleic acids and proteins may be used to diagnose diseases in which the tdk polypeptides are expressed, such as infection by Streptococcus pneumoniae. For example the nucleic acids may be used as probes to detect complementary sequences in sample and the proteins may be used to produce antibodies against (I) (i.e. (VIII)) for use in ELISA tests to detect and quantify the presence of tdk proteins in samples. The proteins may also be used to screen for agonists (X) and antagonists (XI) of the tdk polypeptides which may be used, respectively, to enhance its activity or to treat Streptococcal infections.

L22 ANSWER 18 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2000-491237 [43] WPIDS

DOC. NO. CPI: C2000-147692

TITLE: New Streptococcus pneumoniae MurA polynucleotide

and MurA polypeptide, useful as diagnostic reagents

in the diagnosis of S. pneumoniae infections.

DERWENT CLASS: B04 D16

INVENTOR(S): HUANG, J; JIANG, X; PAYNE, D; VAN HORN, S; WALLIS,

NG

PATENT ASSIGNEE(S): (HUAN-I) HUANG J; (JIAN-I) JIANG X; (PAYN-I) PAYNE

D; (VHOR-I) VAN HORN S; (WALL-I) WALLIS N G; (SMIK)

SMITHKLINE BEECHAM CORP

COUNTRY COUNT: 20

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2000044779 A1 20000803 (200043)\* EN 36

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: JP

US 6346396 B1 20020212 (200219)

# APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 200004477	79 A1	WO 2000-US1307	20000120
US 6346396	B1	US 1999-240936	19990129

PRIORITY APPLN. INFO: US 1999-240936 19990129

AN 2000-491237 [43] WPIDS

AB WO 200044779 A UPAB: 20000907

NOVELTY - Streptococcus pneumoniae MurA polynucleotide (1260 nucleotide sequence (I)) and MurA polypeptide (419 amino acid sequence (II)), are new. Both sequences are defined in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polypeptide (P1) selected from:

(a) an isolated polypeptide comprising an amino acid having at least 95 % identity to (II) over its entire length;

- (b) an isolated polypeptide comprising the amino acid sequence of (II);
  - (c) an isolated polypeptide that is (II); or
- (d) a polypeptide that is encoded by a recombinant polynucleotide comprising the sequence of (I);
  - (2) an isolated polynucleotide (N1) selected from:
- (a) an isolated polynucleotide comprising a sequence encoding a polypeptide that has at least 95 % identity to the sequence of (II) over the entire length;
- (b) an isolated polynucleotide comprising a sequence that has at least 95 % identity over its entire length to a sequence encoding (II);
- (c) an isolated polynucleotide comprising a nucleotide sequence that has at least 95% identity to the sequence of (I) over its entire length;
- (d) an isolated polynucleotide comprising a nucleotide sequence encoding (II);
  - (e) an isolated polynucleotide that is (I);
- (f) an isolated polynucleotide, of at least 30 nucleotides in length obtainable by screening an appropriate library under stringent hybridization conditions with a probe, 30 nucleotides in length, having the sequence of (I) or its fragment;
- (g) an isolated polynucleotide encoding a mature polypeptide expressed by the MurA gene of Streptococcus pneumoniae; or
- (h) a polynucleotide sequence complementary to the isolated polynucleotides of (a) to (g);
  - (3) a method for the treatment of an individual:
- (a) in need of enhanced activity or expression of or immunological response to P1, comprising administering an effective amount of an antagonist to the polypeptide; or
- (b) having need to inhibit activity or expression of P1 comprising:
- (a) administering an effective amount of an antagonist to the polypeptide;
- (b) administering a nucleic acid molecule that inhibits the expression of a polynucleotide sequence encoding the polypeptide;
- (c) administering an effective amount of a polypeptide that competes with Pl for its ligand, substrate, or receptor; or
- (d) administering a polypeptide that induces an immunological response to P1;
- (4) a **process** for diagnosing or prognosing a disease or a susceptibility to a disease related to expression or activity of Pl in an individual, comprising:
- (a) determining the presence or absence of a mutation in the nucleotide sequence encoding the polypeptide; or
- (b) analyzing for the presence or amount of the polypeptide expression in a sample derived from the individual;
- (5) a **process** for producing a polypeptide, comprising culturing a host cell under conditions sufficient for the production of the polypeptide, where the polypeptide is P1;
- (6) a **process** for producing a host cell containing an expression system or its membrane expressing P1, comprising transforming or transfecting the cell with an expression system comprising a polynucleotide encoding P1;
  - (7) a host cell or a membrane expressing P1;
  - (8) an antibody immunospecific for P1;
- (9) a method for screening to identify compounds that agonize or that inhibit the function of P1, comprising a method selected

from:

- (a) measuring the binding of a candidate compound to the polypeptide (or to the cells or membranes bearing the polypeptide) or its fusion protein by means of a label directly or indirectly associated with the candidate compound;
- (b) measuring the binding of a candidate compound to the polypeptide (or to the cells or membranes bearing the polypeptide) or its fusion protein in the presence of a labeled competitor;
- (c) testing whether the candidate compound results in a signal generated by activation or inhibition of the polypeptide, using detection systems appropriate to the cells or cell membranes bearing the polypeptide;
- (d) mixing a candidate compound with a solution comprising P1, to form a mixture, measuring activity of the polypeptide in the mixture, and comparing the activity of the mixture to a standard; or
- (e) detecting the effect of a candidate compound on the production of mRNA encoding the polypeptide and the polypeptide in cells, using for instance, an Enzyme linked immunoabsorbant assay (ELISA) assay; and
  - (10) an agonist or antagonist to P1.

ACTIVITY - Antibacterial; antiinflammatory; antiulcer.

No biological data given.

MECHANISM OF ACTION - MurA antagonist and agonist.

USE - The MurA polynucleotide and polypeptide are useful as diagnostic reagents in the diagnosis of bacterial infections, preferably S. pneumoniae infections.

The agonists and antagonists of the MurA polypeptide are useful in the treatment of Helicobacter pylori infection, gastric ulcers and gastritis. Dwg.0/0

L22 ANSWER 19 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

2000-425477 [37] WPIDS

DOC. NO. CPI:

C2000-129085

TITLE:

Streptococcus pneumoniae polynucleotide and

polypeptide sequences, useful to inhibit and treat bacterial infections, particularly S.

pneumoniae infections.

DERWENT CLASS:

B04 D16

INVENTOR(S):

ALTIERI, M; DOMENICI, E; FAGGIONI, F; FERRARI, L; MOTTI, H; PICCOLI, L; POLISSI, A; PONTIGGIA, A;

PG

RATTI, E; SIMON, D

PATENT ASSIGNEE(S):

(GLAX) GLAXO GROUP LTD

COUNTRY COUNT:

PATENT INFORMATION:

PATENT NO

WEEK

GB 2345288 A 20000705 (200037)\*

KIND DATE

APPLICATION DETAILS:

KIND APPLICATION DATE PATENT NO GB 2345288 · A GB 1998-21362 19981002

> Shears 308-4994 Searcher :

T.A

PRIORITY APPLN. INFO: GB 1998-21362 19981002

AN 2000-425477 [37] WPIDS

AB GB 2345288 A UPAB: 20000807

NOVELTY - An isolated polynucleotide comprising a polynucleotide encoding the 1153, 737, 230, or 248 residue Streptococcus pneumoniae amino acid sequences given in the specification, is new.

DETAILED DESCRIPTION - An isolated polynucleotide comprises:

- (a) a polynucleotide encoding a polypeptide having at least 70% identity to the 1153, 737, 230, or 248 residue amino acid sequences given in the specification;
- (b) a polynucleotide which is complementary to the polynucleotide of (a); and
- (c) a polynucleotide comprising at least 15 sequential bases of the polynucleotide of (a) or (b).

INDEPENDENT CLAIMS are also included for the following:

- (1) a vector comprising the above DNA;
- (2) a host cell comprising the vector of (1);
- (3) producing a polypeptide, comprising, expressing from the host cell of (2) a polypeptide encoded by the DNA;
- (4) producing a cell which expresses a polypeptide comprising transforming or transfecting the cell with the vector of (1) such that the cell expresses the polypeptide encoded by the DNA contained in the vector;
- (5) a polypeptide comprising an amino acid sequence which is at least 70% identical to, or is the 1153, 737, 230, or 248 residue amino acid sequences;
  - (6) an antibody against the polypeptide of (5);
- (7) an antagonist which inhibits the activity of the polypeptide of (5);
- (8) treatment of an individual having need to inhibit the activity of the polypeptide of (6), comprising administering to the individual a therapeutically effective amount of the antagonist of (7);
- (9) a complex of a polypeptide and a binding molecule which comprises the polypeptide of (5) and a binding molecule that is capable of antagonizing the activity of the polypeptide;
- (10) diagnosing a disease related to expression of the polypeptide of (5) comprising determining a nucleic acid sequence encoding the polypeptide;
- (11) a diagnostic **process** comprising analyzing for the presence of the polypeptide of (5) in a sample derived from a host;
- (12) identifying compounds which inhibit the activity of the polypeptide of (5) comprising contacting a cell expressing the polypeptide on its surface with a compound under conditions to permit binding of the polypeptide in the presence of a component capable of providing a detectable signal in response to the binding of the compound to the polypeptide; and determining whether the compound inhibits the binding by detecting the presence of absence of a signal generated from the interaction of the compound with the binding;
- (13) inducing an immunological response in a mammal which comprises inoculating the mammal with the polypeptide of (5) or a fragment or variant of it adequate to protect the animal against infection from S. pneumoniae; and
- (14) inducing an immunological response in a mammal comprising delivering a gene encoding the polypeptide of (5) or a fragment or variant of it, and obtaining expression of the gene in vivo in order

to induce an immunological response to produce antibody to protect the animal against infection from S. pneumoniae.

ACTIVITY - Immunostimulant; Antibacterial.

MECHANISM OF ACTION - None given.

USE - The DNA sequence can be used in a vector used to transfect a host cell to produce the polypeptide. The antagonist can be administered to treat an individual in need of inhibition of the polypeptide. The gene and polypeptide can be used to induce an immunological response in a mammal to protect the animal against infection from S. pneumoniae (all claimed). The sequences and antibodies can also be used to inhibit and/or treat bacterial infections as well as S. pneumoniae infections.

Dwg.0/0

L22 ANSWER 20 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2000-387560 [33] WPIDS

DOC. NO. NON-CPI: N2000-290184 DOC. NO. CPI: C2000-117586

TITLE: New DnaB polypeptide from Streptococcus pneumoniae,

useful, e.g. in vaccines, for diagnosis of infections, and for identifying antibacterial

agents.

DERWENT CLASS: B04 D16 T01

INVENTOR(S): CHALKER, A F; HOLMES, D J; INGRAHAM, K A; JAWORSKI,

D D; LENOX, A L; MAY, E W; MAZZULLA, M J; RAY, J; WANG, M; WARREN, R L; LENNOX, A L; MAZZULLA, M

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP

COUNTRY COUNT: 20

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2000028820 A1 20000525 (200033)\* EN 59

RW: AT BE CH CY DE DK ES FI FR GR GR IE IT LU MC NL PT SE

W: JP

US 6204014 B1 20010320 (200118)

#### APPLICATION DETAILS:

IIII DINI NO IN	IND		PLICATION	DATE
WO 2000028820 US 6204014		WO	1999-US26893	

PRIORITY APPLN. INFO: US 1998-191879 19981113

AN 2000-387560 [33] WPIDS

AB WO 200028820 A UPAB: 20000712

NOVELTY - Isolated DnaB polypeptide (I) that is at least 70% identical with a 450 residue amino acid sequence, fully defined in the specification, over the entire length of it, comprises, or is, the 450 residue sequence, or is encoded by a recombinant polynucleotide comprising a 1953 base pair sequence, fully defined in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for

the following:

- (1) polynucleotide (II) that
- (a) encodes the sequence, at least 70% identical to the 450 residue sequence;
- (b) is at least 70% identical with a sequence encoding the 450 residue sequence;
- (c) is at least 70% identical with the 1953 base pair sequence over the entire 301-1651 nucleotide (nt) segment of it;
  - (d) encodes the 450 residue sequence;
  - (e) is the 301-1651 nt segment of the 1953 base pair sequence;
- (f) is isolated by screening a library, under stringent conditions, with the 1953 base pair sequence, or a fragment of it;
- (g) encodes a mature polypeptide expressed by the DnaB gene of Streptococcus pneumoniae; or
  - (h) is a complement of (a)-(g);
  - (2) antibody (Ab) immunospecific for (I);
- (3) diagnosis or prognosis of disease, or susceptibility, related to expression or activity of (I), comprising determining the presence or absence of a mutation in the nucleotide sequence encoding the polypeptide in the genome of the individual, and analyzing for the presence or amount of the polypeptide expression in a sample derived from the individual;
- (4) screening methods for identifying compounds (A) that activate or inhibit function of (I), comprising:
- (a) measuring the binding of a candidate compound to the polypeptide, or to cells or membranes bearing the polypeptide or a fusion protein of it, using a label directly or indirectly associated with the candidate compound;
- (b) measuring the binding of a candidate compound to the polypeptide or to the cells or membranes bearing the polypeptide or a fusion protein of it, in the presence of a labeled competitor;
- (c) testing if the candidate compound results in a signal generated by activation or inhibition of the polypeptide;
- (d) mixing a candidate compound with a solution containing (I), measuring the activity of the polypeptide, and comparing it to a standard;
- (e) detecting the effect of a candidate compound on the production of mRNA encoding the polypeptide, and the polypeptide in cells, using e.g. enzyme linked immunosorbant assay (ELISA); or
- (f) contacting a composition comprising the polypeptide with the compound to be screened to assess the interaction, the interaction being associated with a second component capable of providing a detectable signal in response to the interaction of the polypeptide and compound, and determining if interaction occurs;
- (5) agonists and antagonists of the expression or activity of (I);
  - (6) expression system comprising (II), present in a host cell;
- (7) host cell, or its membrane, that contains the system of (6) and expresses (I);
  - (8) production of (I) by culturing cells of (7);
- (9) production of cells of (7), or its membranes, by transformation or transfection;
- (10) computer-readable medium containing at least the 450 residue sequence and/or the 1953 base pair sequence;
- (11) computer-based **method** of homology identification, based on the 1953 base pair sequence;
- (12) computer-based method of polynucleotide assembly based on identification of an overlap between the 1953 base pair

sequence, and a second nucleic acid sequence; and (13) polynucleotides of formula (IIa) X-(R1)m-R2-(R3)m-Y (IIa)

X and Y = hydrogen, metal, modified nucleotide or together form
a covalent bond;

each R1 and R3 = optionally modified nucleotide; m and n = 0-3000;

R2 = optionally modified 1953 base pair sequence.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Inhibition of DnaB, probably a replicative helicase, which is essential for growth and/or survival of S. pneumoniae.

USE - The 450 residue polypeptide, the product of the DnaB gene of Streptococcus pneumoniae, is used to screen for specific agonists and antagonists, potential therapeutic agents, to raise specific antibodies (Ab), in vaccines, and in rational drug design. Ab are useful as diagnostic immunoassay reagents and as therapeutic antagonists. Nucleic acids (II) that encode (I), or fragments, are used for recombinant production of (I), and as probes and primers to isolate homologous full-length or genomic clones, for diagnosis, prognosis, staging and typing infections, including detection of genomic mutations, and for chromosome identification or mapping. (II) can also be used in genetic immunization, and as antisense inhibitors. The therapeutic agents have bacteriostatic/bactericidal activity and are used to treat or prevent infections, especially those caused by S. pneumoniae, but also Helicobacter pylori infections and associated disorders, also for treatment of in-dwelling devices and wounds to prevent bacterial adhesion. Dwq.0/0

L22 ANSWER 21 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

2000-318449 [28] WPIDS

DOC. NO. NON-CPI:

N2000-238930 C2000-096569

DOC. NO. CPI: TITLE:

New MurF polypeptide from Streptococcus pneumoniae,

useful e.g. in vaccines, for production of diagnostic antibodies and in screening for

antibacterial agents.

DERWENT CLASS:

B04 D16 J04 S03

INVENTOR(S):

WALLIS, N G

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE .

BEECHAM PLC; (WALL-I) WALLIS N G

COUNTRY COUNT:

28

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG							
CA 2244954	A1	19990325	(200028)	 * EN	64							
JP 11225780	Α	19990824	(200028)		35							
EP 1038962	A1	20000927	(200053)	# EN								
R: AL AT	BE (	CH CY DE	DK ES FI	FR GB	GR IE	ΙT	LΙ	LT	LU	LV	MC	MK
NL PT	RO S	SE SI										
US 6194170	В1	20010227	(200114)									
US 200101633	4 A1	20010823	(200151)									

## APPLICATION DETAILS:

PATENT NO KIND

APPLICATION

DATE

Searcher

Shears

308-4994

CA 2244954	A1	CA 1998-2244954	19980924
JP 11225780	A	JP 1998-309359	19980925
EP 1038962	A1	EP 1999-301987	19990315
US 6194170	B1 Provisional	US 1997-60011P	19970925
		US 1998-143954	19980831
US 2001016334	Al Provisional	US 1997-60011P	19970925
	Div ex	US 1998-143954	19980831
	•	US 2001-754446	20010104

#### FILING DETAILS:

PATENT NO KIND		PA	TENT NO
US 2001016334 A1	Div ex		 6194170

PRIORITY APPLN. INFO: US 1997-60011P 19970925; EP 1999-301987 19990315; US 1998-143954 19980831; US 2001-754446 20010104

AN 2000-318449 [28] WPIDS

AB CA 2244954 A UPAB: 20000613

NOVELTY - New MurF polypeptide from Streptococcus pneumoniae.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) isolated polypeptide (I) comprising a sequence at least 70% identical with a 457 amino acid (aa) sequence (S2), defined in the specification, over its entire length;
  - (2) isolated polynucleotide (II) that:
- (i) encodes (I);
- (ii) has at least 70% identity with (i) over the entire coding region;
- (iii) has at least 70% identity with a sequence of 1702 bp
  (S1), defined in the specification, over its entire length;
- (iv) is produced by screening a library under stringent conditions with a labeled probe comprising at least part of (S1); and
  - (v) is the complement of (i)-(iv);
- (3) expression system, present in a host cell, containing a polynucleotide that expresses (I);
  - (4) host cell, or its membrane, containing the system of (3);
  - (5) production of (I) by culturing cells of (4);
  - (6) antibody (Ab) immunospecific for (I);
  - (7) method for identifying compounds (A) that
- stimulate or inhibit activity of (I);
  (8) agonists and antagonists of (I);
- (9) method for diagnosing disease (or susceptibility) associated with expression of (I);
- (10) isolated polynucleotide (IIa) with at least 70% identity with a sequence of 1676 bp (S3), defined in the specification, over its entire length and able to encode a polypeptide (Ia) with at least 70% identity with a 448 aa sequence (S4), defined in the specification, over its entire length; and
- (11) polypeptide (Ia) with at least 70% identity with (S4) or encoded by (S3).

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Vaccine.

(I) is the UDP-N-acetylmuramoyl-L-Alanyl-D-Glutamyl-L-Lysine:D-Alanyl-D-Alanine ligase of Streptococcus pneumoniae involved in

peptidoglycan biosynthesis and is probably essential for bacterial survival.

USE - (I), the MurF polypeptide of Streptococcus pneumoniae, is used to screen for agents (agonists and antagonists) useful for treating (I)-related
diseases, particularly bacterial infection, especially by S. pneumoniae, but also by Helicobacter pylori.

(I), or its fragments, are also used in vaccines and to raise specific antibodies (Ab). Ab are used for diagnostic detection of (I) in immunoassays, to identify (I)-expressing clones, for affinity purification and as therapeutic agents against infection, including treatment of in-dwelling devices such as catheters and wounds to inhibit bacterial adhesion.

Detection of (I), or the nucleic acid (II) encoding it, is used for diagnosing and staging disease and to monitor response to treatments. (II) is also used for recombinant production of (I) while its fragments are used as probes for detecting mutations, for identification, classification and chromosome detection, in usual hybridization or amplification assays. (II) may also be used in gene vaccines and its antisense or triplex-forming sequences are used therapeutically. Dwg.0/0

L22 ANSWER 22 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

2000-303799 [26] WPIDS

DOC. NO. NON-CPI:

N2000-226936

DOC. NO. CPI:

C2000-092318

B04 D16 S03

TITLE:

Methods for identifying an antibacterial agent for treating Streptococcus pneumoniae infections comprises detecting an interaction between a yneS polypeptide and a test compound.

DERWENT CLASS:

INVENTOR(S):

FRITZ, C; GUZMAN, L; YOUNGMAN, P (MILL-N) MILLENNIUM PHARM INC

PATENT ASSIGNEE(S): COUNTRY COUNT:

PATENT INFORMATION:

KIND DATE PG PATENT NO WEEK LA

87

WO 2000020627 A1 20000413 (200026)\* EN 65

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZW

AU 9962772 A 20000426 (200036)

## APPLICATION DETAILS:

PATENT NO K	IND		PLICATION	DATE
WO 2000020627 AU 9962772	A1	WO	1999-US22665 1999-62772	

## FILING DETAILS:

PATENT NO KIND PATENT NO

AU 9962772 A Based on WO 200020627

PRIORITY APPLN. INFO: US 1998-163445 19980930

AN 2000-303799 [26] WPIDS

AB WO 200020627 A UPAB: 20000531

NOVELTY - Identifying an antibacterial agent comprises contacting a yneS polypeptide from Streptococcus pneumoniae (S-yneS) with a test compound and detecting an interaction of the test compound with the S-yneS polypeptide which indicates that the compound is an antibacterial agent.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

- (1) a method for identifying an antibacterial agent comprising contacting a S-yneS polypeptide with a test compound and detecting a decrease in function of the polypeptide contacted with the test compound and determining whether the compound inhibits growth of bacteria, relative to the growth of bacteria cultured in the absence of a test compound where inhibition of growth indicates the compound is an antibacterial agent;
- (2) a method for identifying an antibacterial agent comprising contacting a nucleic acid encoding S-yneS with a test compound and detecting an interaction of the test compound with the nucleic acid, where an interaction indicates the test compound is an antibacterial agent;
- (3) use of an inhibitor of the function of an S-yneS polypeptide in the preparation of a medicament for treating a Streptococcus pneumoniae infection in a mammal; and
- (4) use of a bacterial agent identified by the above methods in the preparation of a medicament for treating a Streptococcus pneumoniae infection in an organism.

ACTIVITY - Antibacterial. No biological data is given.

MECHANISM OF ACTION - Inhibitor of yneS activity or transcription of a yneS gene or translation of mRNA transcribed from the yneS gene.

USE - The methods are used for identifying antibacterial agents which can be used to prepare compositions and formulations for treating Streptococcus pneumoniae infections in organisms, particularly in mammals e.g. human or rodent (claimed).

ADVANTAGE - yneS is an essential gene for survival of gram negative bacteria making it an ideal candidate for assays detecting antibacterial agents with a broad spectrum of antibacterial activity.

The assays are suitable for high throughput screening of candidate antibacterial agents.  $\ensuremath{\mathsf{Dwg.0/4}}$ 

L22 ANSWER 23 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

2000-271412 [23] WPIDS

DOC. NO. CPI:

C2000-082904

TITLE:

Streptococcus pneumoniae topA polynucleotides and polypeptides, useful as vaccines for treating S.

pneumoniae infection.

DERWENT CLASS:

B04 D16

INVENTOR(S):

GWYNN, M; KALLENDER, H; KATZ, L; SYLVESTER, D;

TRAINI, C M; WARREN, R L; KATZ, L K

Searcher: Shears 308-4994

Just

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM; (SMIK) SMITHKLINE

BEECHAM CORP

COUNTRY COUNT:

21

PATENT INFORMATION:

PATENT	NO	KIND	DATE	WEEK	LA	PG

WO 2000015769 A1 20000323 (200023)\* EN 60

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: JP

EP 1114145 A1 20010711 (200140) EN

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

US 6331411 B1 20011218 (200205)

# APPLICATION DETAILS:

	IND	APPLICATION	DATE
WO 2000015769		WO 1999-US20296	19990902
EP 1114145	Δ1	EP 1999-951401	19990902
		WO 1999-US20296	19990902
US 6331411	B1 CIP of	US 1997-949637	19971014
		US 1998-153277	19980915

#### FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1114145	Al Based on	WO 200015769
US 6331411	B1 CIP of	US 5910414

PRIORITY APPLN. INFO: US 1998-153277 19980915; US 1997-949637 19971014

AN 2000-271412 [23] WPIDS

AB WO 200015769 A UPAB: 20000516

NOVELTY - A 2183 base pair (bp) Streptococcus pneumoniae topA polynucleotide (I) (sequence defined and given in the specification), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a polypeptide (Ia) comprising a defined 695 amino acid sequence (given in the specification) encoded by (I);
- (2) a defined 1524 bp polynucleotide (II) (given in the specification) comprising the S. pneumoniae open reading frame (ORF);
- (3) a polypeptide (IIa) comprising a defined 507 amino acid sequence (given in the specification) encoded by (II);
- (4) polynucleotides and polypeptides with at least 70% identity to (I) or (II) and fragments or variants of (I) or (II);
  - (5) an antibody to (Ia) or (IIa);
- (6) a method for the treatment of an individual requiring enhanced or reduced expression of (Ia) or (IIa) comprising administering (I) or (II) (for enhanced expression) or an antagonist to (Ia) or (IIa) (reduced expression);
- (7) a method for diagnosing a disease or susceptibility to a disease related to expression or activity of (Ia) or (IIa) comprising:
  - (a) determining the presence or absence of a mutation in (I) or

(II); or

(b) analyzing the presence and or quantity of (Ia) or (IIa) in a sample;

(8) a method for screening to identify compounds that activate or inhibit the function of (Ia) or (IIa) comprising:

(a) measuring the binding of a candidate compound to (Ia) or (IIa) using a label directly associated with the candidate compound;

(b) measuring the binding of a candidate compound to (Ia) or

(IIa) in the presence of a labeled competitor;

(c) testing whether the candidate compound results in a signal generated by activation or inhibition of the polypeptide; or

(d) detecting the effect of a candidate compound on the production of mRNA encoding (Ia) or (IIa);

(9) an agonist or antagonist of (Ia) or (IIa);

(10) an expression system comprising (I) or (II);

(11) a host cell comprising the expression system of (10);

(12) a process for producing (Ia) or (IIa) comprising culturing the cell of (11);

(13) a computer readable medium comprising (I), (Ia), (II) and/or (IIa);

(14) a computer based method for performing homology identification comprising providing (I) and/or (II) in a computer readable medium; and

(15) a computer based method for polynucleotide assembly comprising providing (I) and/or (II) in a computer readable medium and screening for at least 1 overlapping region between polynucleotides.

ACTIVITY - Antibacterial. No biological data given. MECHANISM OF ACTION - Vaccine.

USE - (I), (Ia), (II), (IIa), and agonists or antagonists to them, are useful for detecting and/or treating diseases associated with altered levels of topA polypeptides and as vaccines for raising an immune response against S. pneumoniae infection. The polynucleotides and polypeptides may also be used in the discovery and development of antibacterial compounds. Dwq.0/0

WPIDS (C) 2002 THOMSON DERWENT L22 ANSWER 24 OF 49

ACCESSION NUMBER: 2000-256579 [22] WPIDS

C2000-078250 DOC. NO. CPI:

Streptococcus pneumoniae ratC polypeptide and TITLE: polynucleotide useful for treating bacterial infections, especially meningitis and pneumonia.

DERWENT CLASS: B04 D16

KALLENDER, H INVENTOR(S):

(SMIK) SMITHKLINE BEECHAM CORP PATENT ASSIGNEE(S):

COUNTRY COUNT: 20

PATENT INFORMATION:

KIND DATE PG PATENT NO WEEK LA

WO 2000012531 A1 20000309 (200022)\* EN 60

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: JP

EP 1107977 A1 20010620 (200135) EN

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

#### APPLICATION DETAILS:

PATENT NO K	IND	API	PLICATION	DATE
WO 2000012531 EP 1107977		EP	1999-US18701 1999-941199 1999-US18701	19990817

#### FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1107977	Al Based on	WO 200012531

PRIORITY APPLN. INFO: US 1998-140580 19980827

WPIDS 2000-256579 [22]

WO 200012531 A UPAB: 20000508 AB

NOVELTY - An isolated polypeptide (I) comprising a sequence with at least 95% identity to the 100 amino acid sequence, fully defined in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for

the following:

- (1) an isolated polynucleotide (II), encoding comprising a sequence with at least 95% identity to a 303 base pair sequence encoding the 100 amino acid sequence given in the specification;
  - (2) an antisense sequence (III) to (II);
  - (3) an antibody antigenic to or immunospecific for (I);
  - (4) an agonist or antagonist of (I);
  - (5) an expression system (IV) comprising (II);
- (6) a host cell (V) comprising (IV) or a membrane of (IV) expressing (I);
  - (7) producing (I);
  - (8) producing (V); and
- (9) a computer readable medium (VI) having stored on it a member selected from (I), (II), a set of (I) or (II) or a data set representing (I) or (II).

ACTIVITY - Antibacterial; opthalmological; antiinflammatory; auditory.

MECHANISM OF ACTION - Gene therapy; vaccine.

USE - (I) may be used to screen for its agonists and antagonists by contacting (I) with the candidate compound and detecting any alteration in activity of (I) or in a label attached to the candidate. Alternatively, the effect of a candidate compound on the production of mRNA encoding (I) may be detected using an ELISA (Enzyme Linked Immunosorbant Assay) assay (both claimed). Agonists of (I) may be administered to patients to treat conditions associated with increased expression or activity of (I). Agonists of (I) may similarly be used to treat conditions associated with decreased expression or activity of (I) (both claimed). Diseases or conditions arising from altered expression or activity of (I) may be diagnosed by detecting (I) in a sample from a patient or detecting a mutation in (II) in the genome of the patient (claimed). These diseases or conditions include bacterial infections, especially Streptococcus pneumoniae infections, and Helicobacter pylori infections, otitis media,

conjunctivitis, pneumonia, bacteremia, meningitis, sinusitis,

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pleural empyema and endocarditis. (VI) may be used in a computer based method for performing homology identification, comprising providing (II) in (VI) and comparing the polynucleotide sequence to at least one polynucleotide or polypeptide sequence to identify homology (claimed). (II) and (VI) are also used in a computer base method for polynucleotide assembly, comprising providing (II) in (VI) and screening for at least one overlapping region between a the first and a second polynucleotide sequence (claimed).

Dwg.0/0

L22 ANSWER 25 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2

2000-195301 [17] WPIDS

DOC. NO. NON-CPI: DOC. NO. CPI:

N2000-144461 C2000-060591

TITLE:

Streptococcal proteins and polynucleotides useful

for diagnosis, treatment and prophylaxis of

bacterial infections.

DERWENT CLASS:

B04 D16 S03

INVENTOR(S):

HANNIFFY, S B; HANSBRO, P M; LE PAGE, R W F; WELLS,

J M

22

PATENT ASSIGNEE(S):

(MICR-N) MICROBIAL TECHNICS LTD

COUNTRY COUNT:

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2000006738 A2 20000210 (200017) \* EN 76

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: CN JP US

EP 1144640 A2 20011017 (200169) EN

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

CN 1318103 A 20011017 (200213)

# APPLICATION DETAILS:

PATENT NO KIND APPLICATION	DATE
WO 2000006738 A2 WO 1999-GB24	52 19990727
EP 1144640 A2 EP 1999-9349	90 19990727
WC 1999-GB24	52 19990727
CN 1318103 A CN 1999-8109	78 19990727

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1144640	A2 Based on	WO 200006738

PRIORITY APPLN. INFO: US 1999-125329P 19990319; GB 1998-16336 19980727

AN 2000-195301 [17] WPIDS

AB WO 200006738 A UPAB: 20000405

NOVELTY - Streptococcus pneumoniae protein or polypeptide (I), its homologs or derivatives, with a fully defined sequence amino acids (given in the specification), is new.

DETAILED DESCRIPTION - (I) has an amino acid sequence selected from 12 sequences given in the specification.

INDEPENDENT CLAIMS are also included for the following:

(1) a protein or polypeptide (II), its homologs or derivatives having a defined amino acid sequence selected from 61 sequences given in the specification;

(2) an antigenic and/or immunogenic fragment of (I), (II) or a protein or polypeptide (III) having a sequence selected from 12 sequences of defined amino acids given in the specification;

- (3) a nucleic acid molecule (IV) encoding (I), (II) or (III) having defined DNA sequences given in the specification (or their RNA equivalents, complementary sequences, homologs, derivatives or identical sequences);
- (4) an immunogenic and/or antigenic composition (V) comprising(I), (II) or (III) or homologs, derivatives and/or fragments;

(5) a vaccine composition comprising (III);

- (6) an antibody (VI) capable of binding to (I), (II), (III) or a homolog, derivative or fragment; and
- (7) determining the anti-microbial activity of (I) (II) and (III) by inactivating the protein and determining the viability of S.pneumoniae.

ACTIVITY - Antiinflammatory; antibacterial. MECHANISM OF ACTION - Vaccine; antagonist.

100 micro g of recombinant pcDNA3.1 (IV) was injected intramuscularly into the tibialis anterior muscle of both legs of mice. A booster dose was given 4 weeks later and control groups received either non-recombinant pcDNA3.1+DNA or no vaccine. After the second immunization, all mice groups were challenged intra-nasally with a lethal doses of Streptococcus pneumoniae serotype 4 (strain NCTC 11886). Mice were monitored for the development of symptoms associated with the onset of S.pneumoniae induced-disease. The groups vaccinated with DNA survived significantly longer than non-vaccinated controls.

USE - (I) or homologs, derivatives and/or fragments are useful as an immunogen or antigen and (V) is useful as a vaccine and also in a diagnostic assay. (I-V) are useful for detection or diagnosis of S. pneumoniae, by contacting a sample to be tested with them. Agents capable of antagonizing, inhibiting or interfering with the function or expression of the protein or polypeptide (II) are useful in medical compositions in the treatment or prophylaxis of S.pneumoniae infection (claimed).

L22 ANSWER 26 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2000-072185 [06]

DOC. NO. CPI: C2000-020554

TITLE: Novel Streptococcal gcp polynucleotides and

polypeptides useful for screening for antibacterial

compounds.

DERWENT CLASS:

B04 D16

INVENTOR(S):

BISWAS, S; CHALKER, A F; HOLMES, D J; INGRAHAM, K

WPIDS

A; PALMER, L M; RAY, J E; WARREN, R L; ZALACAIN, M;

HOLMES, D

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP

COUNTRY COUNT:

21

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

A2 19991104 (200006) \* EN WO 9955900

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: JP

EP 1073669 A2 20010207 (200109)

R: BE CH DE DK FR GB IT LI NL

US 6274719 B1 20010814 (200148)

82 JP 2002512809 W 20020508 (200234)

#### APPLICATION DETAILS:

PATENT NO K	IND	APPLICATION	ON	DATE
WO 9955900 EP 1073669	A2 A2	WO 1999-U EP 1999-9	20	19990422 19990422
20,000		WO 1999-U		19990422
US 6274719	B1	US 1998-6	6512	19980424
JP 2002512809	W	WO 1999-U	S8770	19990422
		JP 2000-5	46043	19990422

#### FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1073669	A2 Based on	WO 9955900
JP 200251280	9 W Based on	WO 9955900

PRIORITY APPLN. INFO: US 1998-66512 19980424

2000-072185 [06] WPIDS AN

9955900 A UPAB: 20000203 AΒ

NOVELTY - Novel gcp polynucleotides and polypeptides are disclosed.

They are isolated from Streptococcus pneumoniae.

DETAILED DESCRIPTION - An isolated gcp polypeptide (I) is new, and comprises the 336 amino acid sequence (A) given in the specification, or has at least 70 (especially 95) % identity to, and over the entire length of (A).

INDEPENDENT CLAIMS are also included for:

- (1) an isolated gcp polynucleotide (II) selected from:
- (a) an isolated polynucleotide encoding (I);
- (b) an isolated polynucleotide that has at least 70 (especially 95) % identity to, and over the entire length of, the polynucleotide of (a);
- (c) an isolated polynucleotide that has at least 70 (especially 95) % identity 1011 bp sequence (B) given in the specification;
  - (d) an isolated polynucleotide encoding (A);
  - (e) an isolated polynucleotide that comprises (B);
- (f) an isolated polynucleotide obtainable by screening an appropriate library under stringent hybridization conditions with a probe comprising (B) or a fragment;
- (g) an isolated polynucleotide encoding a mature polypeptide expressed by the gcp gene of S. pneumoniae; and
- (h) a polynucleotide sequence complementary to the polynucleotides of (a) to (g);
  - (2) an antibody antigenic to or immunospecific for (I);
- (3) a method for the treatment of an individual in need of enhanced activity or expression of (I);
- (4) a method for the treatment of an individual having need to inhibit activity or expression of (I);
  - (5) a process for diagnosing or prognosis a disease

Shears 308-4994 Searcher :

or a susceptibility to a disease in an individual related to expression or activity of (I);

- (6) a method for screening to identify compounds that activate or that inhibit the function of (I), comprising a method selected from:
- (i) measuring the binding of a candidate compound to (I) or to the cells or membranes bearing (I) or a fusion protein thereof by means of a label directly or indirectly associated with the candidate compound;
- (ii) measuring the binding of a candidate compound to (I) or to the cells or membranes bearing (I) or a fusion protein thereof in the presence of a labeled competitor;
- (iii) testing whether the candidate compound results in a signal generated by activation or inhibition of the polypeptide using detection systems appropriate to the cells or cell membranes bearing (I);
- (iv) mixing a candidate compound with a solution containing(I), to form a mixture measuring activity of the polypeptide in the mixture, and comparing the activity of the mixture to a standard;
- (v) detecting the effect of a candidate compound on the production of mRNA encoding (I), using e.g. an ELISA assay; or
- (vi) contacting a composition comprising (I) with the compound to be screened under conditions permitting interaction between the compound and the polypeptide to assess the interaction of a compound, such interaction being associated with a second component capable of providing a detectable signal in response to the interaction of the polypeptide with the compound; and determining whether the compound interacts with and activates or inhibits an activity of (I) by detecting the presence or absence of a signal generated from the interaction of the compound with (I);
- (7) an agonist or an antagonist of the activity or expression of (I);
  - (8) an expression system comprising a polynucleotide capable of producing (I) when said expression system is present in a compatible host cell;
  - (9) a host cell comprising the expression system of (8) or a membrane thereof expressing (I);
  - (10) a process for producing (I) comprising the step of culturing a host cell of (9) under conditions sufficient for the production of said polypeptide;
  - (11) a process for producing a host cell comprising the expression system of (8), comprising transforming or transfecting a cell with an expression system such that the host cell, under appropriate culture conditions, produces (I);
  - (12) a host cell produced by the **process** of (11) or a membrane thereof expressing (I);
  - (13) a computer readable medium having stored thereon a member selected from the group consisting of:
    - (a) a polynucleotide comprising (B);
    - (b) a polypeptide comprising (A);
  - (c) a set of polynucleotide sequences wherein at least one of the sequences is (B);
  - (d) a set of polypeptide sequences wherein at least one of the sequences comprises (A);
  - (e) a data set representing a polynucleotide sequence comprising the (B);
  - (f) a data set representing a polynucleotide sequence encoding a polypeptide sequence comprising (A);

(14) a computer based method for performing homology identification, comprising providing a polynucleotide sequence comprising (B) in a computer readable medium, and comparing the polynucleotide sequence to at least one polynucleotide or polypeptide sequence to identify homology.

ACTIVITY - Glycopeptidase.

MECHANISM OF ACTION - None given.

USE - GCP polypeptides and polynucleotides are useful for diagnosing diseases due to an infection of an organism with the GCP gene (claimed). They can diagnose the stage and type of infection. GCP polypeptides are also useful for screening for compounds which affect activity of the protein (claimed). These can be used in treatment to inhibit (antagonist i.e. antibacterial drugs) or enhance (agonist) GCP activity, in addition to direct administration of GCP polypeptides to treat conditions associated with a lack of GCP polypeptide (claimed), or direct administration of antisense sequences to prevent expression. GCP polypeptides (administered directly, in a vector i.e. gene therapy, and as a vaccine) and antibodies induce an immune response to immunize and prevent disease. Anti-GCP antibodies induced by the polypeptide are also useful for isolating clones expressing GCP (I), or for purifying the polypeptide by affinity chromatography. Diseases diagnosed, prevented or treated include otitis media, conjunctivitis, pneumonia, bacteremia, sinusitis, pleural empyema, endocarditis and especially meningitis. GCP polypeptides, polynucleotides and their (ant)agonists can to prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection

ADVANTAGE - The frequency of Streptococcal infections has risen dramatically, and it is no longer common to isolate Streptococcus pneumoniae strains that are resistant to standard antibiotics. The gcp products of the invention can be used screen for new antibacterial compounds that may target these resistant bacteria. Dwg.0/0

L22 ANSWER 27 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2000-062670 [05]

DOC. NO. CPI: C2000-017457

TITLE: New isolated priA polypeptides, useful for

screening antibacterial compounds.

WPIDS

DERWENT CLASS: B04 D16

INVENTOR(S): MCDEVITT, D; SHILLING, L K; ST JOHN, A; WARREN, R

L; SHILLING, L

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP

COUNTRY COUNT: 21

COUNTRY COUNT: 2
PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 9961453 A2 19991202 (200005) \* EN 68

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: JP

US 6146846 A 20001114 (200060)

EP 1077983 A2 20010228 (200113) EN

R: BE CH DE DK FR GB IT LI NL

JP 2002516333 W 20020604 (200239) 90

### APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9961453 US 6146846	A2 A	WO 1999-US8771 US 1998-67091	19990422 19980427
EP 1077983	A2	EP 1999-946573 WO 1999-US8771	19990422 19990422
JP 20025163	33 W	WO 1999-US8771 JP 2000-550857	19990422 19990422

# FILING DETAILS:

PATENT NO K	IND	PATENT NO
EP 1077983	A2 Based on	WO 9961453
JP 2002516333	W Based on	WO 9961453

PRIORITY APPLN. INFO: US 1998-67091 19980427

AN 2000-062670 [05] WPIDS

AB WO 9961453 A UPAB: 20000128

NOVELTY - An isolated priA polypeptide (I) is new.

DETAILED DESCRIPTION - (I) comprises:

- (a) an amino acid comprising at least 70-95% identity to an 804 amino acid sequence (A) fully defined in the specification;
  - (b) an isolated polypeptide comprising (A);
  - (c) an isolated polypeptide which is (A); or
- (d) a polypeptide which is encoded by a recombinant polynucleotide (PN) comprising the PN (A).

INDEPENDENT CLAIMS are also included for the following:

- (1) an isolated PN (II) sequence encoding (I);
- (2) an antibody (III) antigenic to or immunospecific to (I);
- (3) treatment of an individual:
- (a) in need of enhanced activity or expression of (I) comprising:
  - (i) administering an agonist to (I); or
- (ii) providing an isolated PN comprising a sequence encoding the polypeptide in a form so as to effect production of the polypeptide activity in vivo; or
- (b) having need to inhibit activity or expression of (I) comprising:
  - (i) administering an antagonist to (I); or
- (ii) administering a nucleic acid molecule that inhibits the expression of a PN sequence encoding (I); or
- (iii) administering a polypeptide that competes with (I) for its ligand, substrate or receptor;
- (4) diagnosing or prognosing a disease or a susceptibility to a disease in an individual related to expression or activity of (I) by:
- (a) determining the presence or absence of a mutation in the nucleotide sequence encoding (I) in the genome; or
- (b) analyzing for the presence or amount of (I) expression in a sample derived from the individual;
- (5) screening to identify compounds that activate or inhibit the function of (I) by:
- (a) measuring the binding of a candidate compound to (I) or to the cells or membranes bearing (I) or a fusion protein by means of a label(in)directly associated with the compound;
  - (b) measuring the binding of a candidate compound to (I) or to

the cells or membranes bearing (I) or a fusion protein in the presence of a labeled competitor;

- (c) testing whether the candidate compound results in a signal generated by activation or inhibition of the polypeptide using detection systems appropriate to the cells or cell membranes bearing (I);
- (d) mixing a candidate compound with a solution containing (I) to form a mixture measuring the activity of (I) in the mixture and comparing the activity of the mixture to a standard;
- (e) detecting the effect of a candidate compound on the production of mRNA encoding the polypeptide and the polypeptide in cells using for instance an ELISA assay, or
- (f) contacting a composition comprising (I) with the compound to be screened to permit interaction between the compound and the polypeptide to assess the interaction of a compound which is associated with a second component capable of providing a detectable signal in response to the interaction of the polypeptide with the compound and determining whether the compound interacts with and activates or inhibits an activity of (I) by detecting the presence or absence of a signal generated from the interaction of the compound with (I);
- (6) an agonist or an antagonist of the activity or expression of (I);
- (7) an expression system (IV) comprising a polynucleotide capable of producing a polypeptide (I) in a compatible host cell;
- (8) a host cell (V) comprising (IV) or a membrane expressing or comprising (I);
  - (9) producing a polypeptide (I) by culturing a host cell;
- (10) production of a host cell comprising the expression system or a membrane expressing (I) by transforming or transfecting a cell with an expression system comprising a polynucleotide capable of producing (I);
- (11) a computer readable medium having stored a member selected from a group comprising a polynucleotide comprising a sequence (S1)-(S5) of 3015, 804, 27, 30 or 2415 base pairs (given in the specification), a polypeptide comprising (A), a set of polynucleotide sequences where at least one of the sequences comprises (S1)-(S5), a set of polypeptide sequences comprising (A), a data set representing a polynucleotide comprising (S1)-(S5), a data set representing a polynucleotide sequence encoding a polypeptide comprising (A), a polynucleotide comprising (S1)-(S5) a set of polypeptide sequences where at least one of the sequences comprises (A), a data set representing a polynucleotide sequence encoding a polypeptide sequence comprising (A), and
- (12) a computer based method for performing homology identification comprising providing a polynucleotide sequence comprising a 3015 base pair sequence (fully defined in the specification) in a computer readable medium and comparing the polynucleotide sequence to at least one polynucleotide or polypeptide sequence to identify homology.

ACTIVITY - Antimicrobial.

MECHANISM OF ACTION - None given.

USE - (I) and polynucleotides are useful for the treatment of microbial diseases (especially in the form of vaccines) and the methods are useful for identifying agonists and antagonists. (I) are also useful for relating to diagnostic assays for detecting diseases associated with microbial infections (especially infections by Streptococcus pneumoniae) and conditions associated with such

infections and assays for detecting priA expression or activity. The polypeptides were useful in the discovery and development of antibacterial compounds. The encoded protein upon expression can be used as a target for screening of antibacterial drugs.

ADVANTAGE - None given.

Dwg.0/0

L22 ANSWER 28 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1999-

1999-265618 [23] WPIDS

DOC. NO. NON-CPI:

N1999-198028

DOC. NO. CPI:

C1999-078427

TITLE:

New aroC gene useful in diagnosing and treating

diseases such as meningitis, pneumonia and

endocarditis.

DERWENT CLASS:

B04 D16 S03 T01

INVENTOR(S):

BISWAS, S; BROWN, J R; BRYANT, A; CHALKER, A F;

HOLMES, D J; INGRAHAM, K A; MARRA, A; PAYNE, D J;

ZALACAIN, M

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP

COUNTRY COUNT:

27

PATENT INFORMATION:

PATENT	NO	KIND	DATE	WEEK	LA	PG

EP 913480 A2 19990506 (199923)\* EN 37

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK

NL PT RO SE SI

CA 2249002 A1 19990503 (199942) EN

JP 2000197482 A 20000718 (200040)# 101

## APPLICATION DETAILS:

PATENT NO K	ÌND	API	PLICATION	DATE
EP 913480	A2	EP	1998-203627	19981026
CA 2249002	A1	CA	1998-2249002	19981029
JP 2000197482	A	JΡ	1998-352054	19981104

PRIORITY APPLN. INFO: US 1997-64039P 19971103; JP 1998-352054 19981104

AN 1999-265618 [23] WPIDS

AB EP 913480 A UPAB: 19990616

NOVELTY - A new polypeptide from Streptococcus pneumoniae has at least 70-95% identity with a fully defined sequence of 338 amino acids and is encoded by the 1167 base recombinant polynucleotide sequence given in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for

the following:

(1) a polynucleotide or its complement (II) comprising:

(a) a polynucleotide encoding a polypeptide with at least 70-95 % identity to the fully defined 338 amino acid sequence; or

(b) a polynucleotide with at least 70-95% identity to the fully defined 1167 base sequence;

(2) an antibody antigenic to or immunospecific for (I);

(3) a method for treating:

(a) an individual requiring (I) comprising administering (II) or an agonist of (I); and

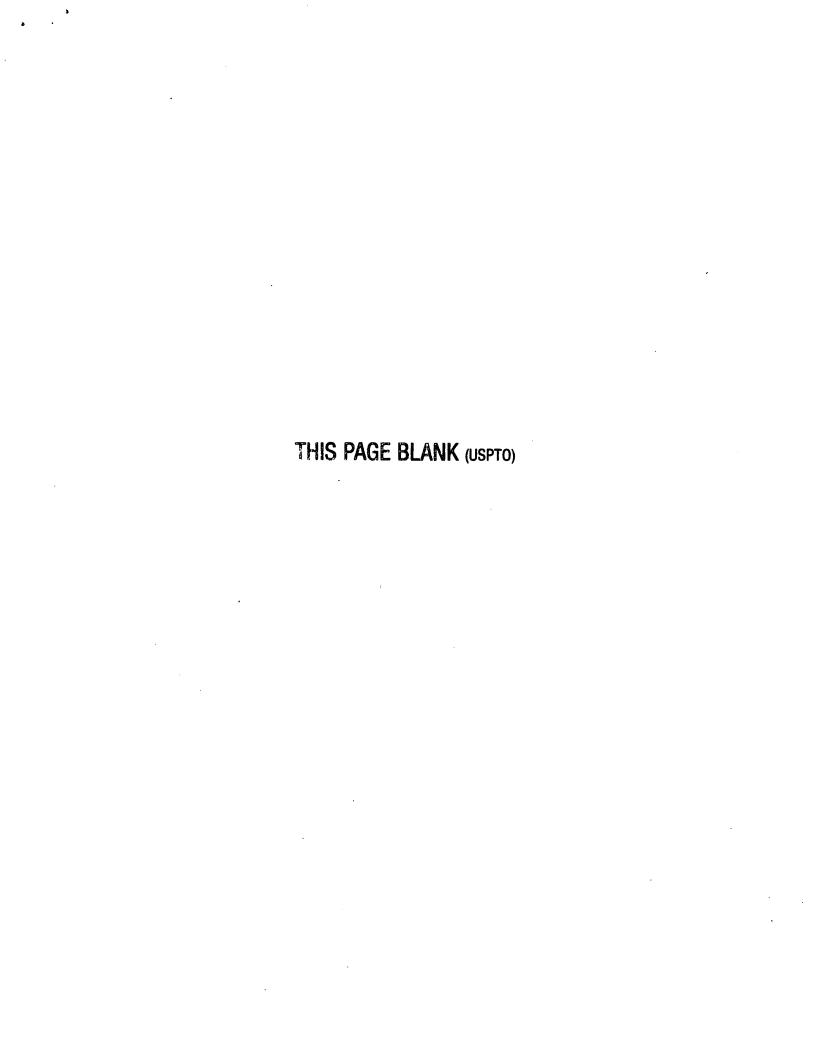
- (b) an individual requiring inhibition of (I) comprising administering an antagonist of (I), a polynucleotide which interferes with expression of (II) or a polypeptide which competes with (I);
  - (4) an agonist or antagonist of (I);
  - (5) an expression system comprising (II) in a host cell (III);
  - (6) (III) or part of its membrane expressing (I);
- (7) a process for producing (I) comprising culturing
  (III);
- (8) a process for producing (III) comprising
  transfecting a cell with (II);
- (9) a database comprising the sequences of (I) and (II); and (10) a computer based homology search comprising searching for sequence overlap between (II) and another sequence.

ACTIVITY - Administered (I), (II) or antibodies or agonists of (I) are antibacterial and anti-inflammatory.

MECHANISM OF ACTION - Administered (I) or (II) provokes an immune response to inhibit endogenous (I). Antagonists of (I) inhibit endogenous (I).

USE - (II) may be administered as gene therapy to allow in vivo expression of (I) in patients. This stimulates an immune response against (I) and protects against infection by Streptococcus pneumoniae. Agonists of (I) may be administered to patients requiring enhanced activity of (I). Similarly antagonists of (I) such as antibodies against (I) may be administered to inhibit activity of (I) in patients. Diseases caused by Streptococcus pneumoniae include meningitis, pneumonia, conjunctivitis, bacteremia, sinusitis and endocarditis. These diseases may be diagnosed by detecting mutation in (II) or detecting the presence of (I) in a sample from a patient. RT-PCR may be used as part of a differential display regime to detect (II) in infected tissue from a patient. (I) may be used to screen for agonists or antagonists of (I) by contacting it with a candidate compound in the presence of a signal system or by monitoring the effect of the compound on production and expression of the mRNA encoding (I). Fusion proteins incorporating (I) and the Fc portion of immunoglobulins may be used in high-throughput screening assays to identify antagonists of (I). (II) may be used as hybridization probes to isolate full length cDNAs encoding (I) or other proteins. (II) may be used for serotyping and taxonomic classification of infecting organisms and to monitor gene expression, genetic linkage and genetic variability. (II) is also useful for chromosome mapping and may be incorporated into polynucleotide arrays for diagnostic and prognostic purposes. Antibodies against (I) may be used to isolate clones expressing (I) by affinity chromatography. (I), (II) and antibodies to (I) may be used to devise screens for compounds which alter expression of the mRNA expressing (I). (I) may also be used to identify membrane-bound or soluble receptors of (I).

Frozen infected tissue samples were placed in a dry ice ethanol bath and 50-100 mg were disrupted with 1 ml of extraction reagents (FastRNA BIO101) in the presence of a silica/ceramic matrix. The samples were shaken in a reciprocating shaker (fastprep FP120, BIO101) at 6000 rpm for 20-120 seconds. The crude RNA was extracted with chloroform/isoamyl alcohol and precipitated with DEPC-treated/isopropanol precipitation solution (BIO101). The RNA was pelleted (12,000 g for 10 minutes), washed with 75% ethanol, air-dried for 5-10 minutes and resuspended in 0.1 ml of DEPC-treated



water, followed by 5-10 minutes at 55oC. After at least 1 minute on ice 200 units of Rnasin was added. DNA was removed from 50 micro g samples by a 30 minute treatment at 37oC with 20 units of RNAase-free DNAasel in the buffer supplied in a final volume of 57 micro 1. The DNAase was inactivated and removed by treatment with TRIzol LS Reagent (Gibco BRL) according to the manufacturers protocol. DNAase-treated RNA was resuspended in 100 micro 1 DEPC-treated water with the addition of Rnasin. 3 micro g samples of DNAase-treated RNA were reverse transcribed using a Superscript Preamplification System for First Strand cDNA Synthesis kit (Gibco BRL) according to the manufacturers instructions. 150 ng of random hexamers were used to prime each reaction. PCR reactions were set up on ice, containing 43 microlitres of PCR Master Mix (Advanced Biotechnologies Ltd.), 1 micro 1 PCR primers at 10 mM initial concentration and 5 micro 1 cDNA. The reactions were run on a Perkin Elmer GeneAmp PCR System 9600. 10 micro 1 aliquots were then run out on 1 % 1 x TBE gels stained with ethidium bromide. The sizes of PCR products are compared to the predicted sizes of RNAs from Streptococcus pneumoniae such as that encoding aroC. The presence of products of the correct size indicates infection with Streptococcus pneumoniae.

ADVANTAGE - Prior art methods of control of Streptococcus pneumoniae involved administration of antibiotics. However the frequency of infections by Streptococcus pneumoniae has risen in recent decades due to multiply resistant strains of this bacterium and increasing numbers of people with weakened immune systems. The new aroC protein is important for viability of Streptococcus pneumoniae so an immune response against it will prevent or ameliorate infection by this organism without the use of antibiotics.

Dwg.0/0

L22 ANSWER 29 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

1999-256632 [22] WPIDS

DOC. NO. NON-CPI:

N1999-191208

DOC. NO. CPI:

C1999-075297

TITLE:

New adenine glycosylase from Streptococcus pneumoniae useful for diagnosing and treating diseases such as meningitis, pneumonia and

endocarditis.

DERWENT CLASS:

B04 D16 S03

INVENTOR(S):

BLACK, M T; BROWN, J R; HODGSON, J E; HOLMES, D J;

KNOWLES, D J C; LONETTO, M A; NICHOLAS, R O;

STODOLA, R K; ZALACAIN, M

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC

COUNTRY COUNT:

27

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

EP 913479 A2 19990506 (199922)\* EN 30

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK

NL PT RO SE SI

CA 2248116 A1 19990427 (199941) EN

JP 11253185 A 19990921 (199950) 70

APPLICATION DETAILS:

PATENT NO F	(IND	APPLICATION	DATE
EP 913479	A2	EP 1998-203504	19981019
CA 2248116	A1	CA 1998-2248116	19981021
JP 11253185	A	JP 1998-344818	19981027

PRIORITY APPLN. INFO: US 1997-958676 19971027

AN 1999-256632 [22] WPIDS

AB EP 913479 A UPAB: 19990609

NOVELTY - A polypeptide (I) is new and has at least 70% identity to the sequence of 391 amino acids given in the specification, which codes for the mutY adenine glycosylase from Streptococcus pneumoniae.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a polynucleotide or its complement (II) at least 15 bases long selected from:
- (a) a polynucleotide with at least 70% identity to a polynucleotide encoding mutY; and
  - (b) a polynucleotide encoding (I);
  - (2) a vector (III) comprising (II);
  - (3) a host cell comprising (III);
- (4) a **process** for producing (I) by expressing it from the host cell;
  - (5) an antibody against (I); and
  - (6) an antagonist of (I).

ACTIVITY - Administered mutY and its antagonists are antibacterial and antiinflammatory.

MECHANISM OF ACTION - Administered muty raises an immune response directed to muty in infecting Streptococcus pneumoniae. Administered antagonists of muty inhibit its activity.

USE - MutY can be used to vaccinate patients and raise an immune response against Streptococcus pneumoniae by administration of the **protein**. MutY **protein** may also be applied to implanted devices, wounds or skin to protect against or **treat Streptococcus pneumoniae** 

infections. Similarly (II) may be administered to a patient to cause in vivo expression of muty which will then stimulate an immune response. Administration of muty or (II) will also protect against Helicobacter pylori infection which causes diseases such as stomach cancer, ulcers and gastritis. Antagonists of muty may be administered to inhibit muty in an infected individual. Diseases such as meningitis, pneumonia, endocarditis, conjunctivitis and sinusitis may be diagnosed by detection of (II) in an individual by RT-PCR, or detecting muty in a cell sample from a patient. Detection of (II) using PCR can also be used to gauge the stage of infection of Streptococcus

pneumoniae as certain bacterial proteins are expressed only at certain stages of infection. Agonists and antagonists of muty may be identified by contacting it with a candidate compound in the presence of a signal system. (II) may be used as hybridization probes to isolate cDNAs encoding muty. Antibodies against muty can be used to identify clones expressing muty by affinity chromatography.

Infected tissue sample were thawed in a dry ice ethanol bath. To disperse the tissue, 50 100 mg were added to a silica/ceramic mix

and 1 ml of extraction agents (FasttRNA BIO101) were added (sample:reagent volume = 1:20). The tubes were shaken in a reciprocating shaker (FastPrep FP120 BIO101) at 6000rpm for 20-120 seconds. The crude RNA preparation was extracted with chloroform/isoamyl alcohol and precipitated with DEPC-treated/Isopropanol Precipitation solution (BIO101). The RNA was pelleted (12000g, 10 minutes), washed with 75% ethanol, air-dried for 5-10 minutes and resuspended in 0.1 ml DEPC-treated water followed by 5-10 minutes at 55oC. After at least 1 minute on ice, 200 units of Rnasin were added. RNA yields were assessed using 1 x TBE gels stained with ethidium bromide. To demonstrate isolation of bacterial RNA from infected tissue 1 x MOPS, 2.2M formaldehyde gels were run and vacuum blotted onto Hybond-N (Amersham). The blots were hybridized with a 32P labelled oligonucleotide probe of sequence 5' AACTGAGACTGGCTTTAAGAGATTA 3', specific to 16S rRNA from Streptococcus pneumoniae. The size of bands arising from hybridization were compared to those of RNA from Streptococcus pneumoniae grown in vitro. Correctly sized rRNA were detected from the infected tissue showing that this may be used as a diagnostic tool.

ADVANTAGE - Prior art methods of controlling bacterial infections involved administration of antibiotics. However many bacterial strains are now resistant to some or all antibiotics. This, along with weakened immune systams in many patients has caused an increase in the number of diseases caused by bacterial infections. The new muty protein is expressed by Streptococcus pneumoniae at specific stages of infection. It is important for bacterial viability as it contributes to the removal of oxidized guanidines from the genome, which can cause mismatches and mutations. Muty and the sequences encoding it can therefore be used to diagnose or prevent bacterial infections without the use of antibiotics.

Dwg.0/0

L22 ANSWER 30 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1999-155938 [14] WPIDS

DOC. NO. NON-CPI: N1999-112678 DOC. NO. CPI: C1999-046117

TITLE: New Streptococcus pneumoniae Histidine Kinase (HK)

polypeptide and polynucleotide - useful as diagnostic reagents and for prevention and

treatment of Streptococci infections, which cause

conjunctivitis, otitis media and meningitis.

DERWENT CLASS: B04 D16 S03 INVENTOR(S): BLACK, M T

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM

COUNTRY COUNT: 28

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG A2 19990310 (199914) \* EN EP 900845 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI 19990303 (199933) CA 2242313 Α 19990831 (199946) 89 JP 11235183 Α B1 20010904 (200154) US 6284515

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 900845 CA 2242313 JP 11235183 US 6284515	A2 A A B1 Provisional	EP 1998-306742 CA 1998-2242313 JP 1998-289963 US 1997-57890P US 1998-35382	19980824 19980825 19980903 19970903 19980305

PRIORITY APPLN. INFO: US 1998-35382 19980305; US 1997-57890P

AN 1999-155938 [14] WPIDS

AB EP 900845 A UPAB: 19990412

NOVELTY - A Streptococcus pneumoniae Histidine Kinase (HK) polypeptide which is a component of the two component signal transduction system (TCSTS) in bacteria, comprises at least 70% identity to sequence (I), a fully defined 560 amino acid protein given in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) an isolated polynucleotide (II) (DNA or RNA) comprising a sequence selected from a polynucleotide which: (i) has 70% identity to a polynucleotide encoding: (a) polypeptide (I); (b) the mature HK polypeptide expressed Streptococcus pneumoniae 0100993; (ii) is complementary to the polynucleotides; and (iii) comprises at least 15 sequential bases of polynucleotides (i) or (ii); (2) a vector comprising polynucleotide (II); (3) a host cell comprising the vector; (4) an antibody immunospecific to HK polypeptide (I); (5) an antagonist which inhibits activity or expression of HK polypeptide (I); and (6) preparation of HK polypeptide (I).

USE - HK polypeptides and polynucleotides are useful for diagnosing diseases related to over or underexpression of HK protein by identifying mutations in the HK gene, or determining HK polypeptide or mRNA expression levels due to an infection of an organism with the HK gene (claimed). They can diagnose the stage and type of infection. HK polypeptides are also useful for screening for compounds which affect activity of the protein by measuring the binding to polypeptide (I) and observing the stimulation or inhibition of the polypeptide function (claimed). These can be used in treatment to inhibit ( antagonist i.e. antibacterial drugs) or enhance (agonist) HK activity, in addition to direct administration of  $\mbox{HK}$ polypeptides to treat conditions associated with a lack of HK polypeptide (claimed), or direct administration of antisense sequences to prevent expression. HK polypeptides (administered directly, in a vector and as a vaccine) and antibodies induce an immune response to immunise and prevent disease (claimed). Diseases diagnosed, prevented or treated include: bacterial infections, especially Streptococcus pneumoniae infections, which cause otitis media, conjunctivitis, bacteremia, sinusitis, pleural empyema, endocarditis and especially meningitis. HK polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are

useful for use on wounds and body implants to prevent bacterial infection.  $\mathsf{Dwg.0/0}$ 

L22 ANSWER 31 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1999-155936 [14]

DOC. NO. NON-CPI: N1999-112677 DOC. NO. CPI: C1999-046115

TITLE: New Streptococcus pneumoniae Fifty-Four Homologue

(Ffh) polypeptide and polynucleotide - useful as

diagnostic reagents and for prevention and

WPIDS

treatment of Streptococci infections, which cause

otitis media, sinusitis and conjunctivitis.

DERWENT CLASS: B04 D16 S03 INVENTOR(S): BLACK, M T

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM

COUNTRY COUNT: 28

PATENT INFORMATION:

EP 900843 A2 19990310 (199914)\* EN 21 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK

NL PT RO SE SI

CA 2241417 A 19990302 (199933) JP 11221087 A 19990817 (199943) 55

US 5972651 A 19991026 (199952) US 6350857 B1 20020226 (200220)

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 900843	A2	EP 1998-306685 CA 1998-2241417	19980820 19980820
CA 2241417 JP 11221087	A A	JP 1998-288632	19980902
US 5972651	A	US 1997-923772	19970902
US 6350857	B1 Div ex	US 1997-923772 US 1999-385287	19970902 19990830

# FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 6350857	B1 Div ex	US 5972651

PRIORITY APPLN. INFO: US 1997-923772 19970902; US 1999-385287

19990830

AN 1999-155936 [14] WPIDS

AB EP 900843 A UPAB: 19990424

NOVELTY - A polypeptide comprises at least 70% identity to sequence (I), a fully defined 523 amino acid Streptococcus pneumoniae Fifty-Four Homologue (Ffh) protein given in the specification, which is a component of the protein secretory apparatus in bacteria, and the bacterial homolgue of the eukaryotic Signal Recognition Particle.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included

for: (1) an isolated polynucleotide (II) (DNA or RNA) comprising a

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sequence selected from a polynucleotide which: (i) has 70% identity
to a polynucleotide encoding: (a) polypeptide (I); (b) the mature
Ffh polypeptide expressed by Streptococcus pneumoniae 0100993; (ii)
is complementary to the polynucleotides; and (iii) comprises at
least 15 sequential bases of polynucleotides (i) or (ii); (2) a
vector comprising polynucleotide (II); (3) a host cell comprising
the vector; (4) an antibody immunospecific to Ffh polypeptide (I);
(5) an antagonist which inhibits activity or expression of Ffh
polypeptide (I); and (6) preparation of Ffh polypeptide (I).
     USE - Ffh. polypeptides and polynucleotides are useful
for diagnosing diseases related to over or underexpression of Ffh
protein by identifying mutations in the Ffh gene, or
determining Ffh polypeptide or mRNA expression levels due
to an infection of an organism with the Ffh gene (claimed). They can
diagnose the stage and type of infection. Ffh polypeptides
are also useful for screening for compounds which affect activity of
the protein by measuring the binding to
polypeptide (I) and observing the stimulation or
inhibition of the polypeptide function (claimed).
These can be used in treatment to inhibit (
antagonist i.e. antibacterial drugs; or enhance
(agonist) Ffh activity, in addition to direct administration of Ffh
polypeptides to treat conditions associated with a
lack of Ffh polypeptide (claimed), or direct
administration of antisense sequences to prevent expression. Ffh
polypeptides (administered directly, in a vector and as a
vaccine) and antibodies induce an immune response to immunise and
prevent disease (claimed). Diseases diagnosed, prevented or
treated include: bacterial infections, especially
Streptococcus pneumoniae infections,
which cause otitis media, conjunctivitis, bacteremia, sinusitis,
pleural empyema, endocarditis and especially meningitis. Ffh
polypeptides, polynucleotides and their (ant)agonists can
prevent adhesion of bacteria to matrix proteins, and are
useful for use on wounds and body implants to prevent bacterial
infection.
Dwg.0/0
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WPIDS (C) 2002 THOMSON DERWENT L22 ANSWER 32 OF 49

ACCESSION NUMBER:

1999-144807 [13] WPIDS

DOC. NO. CPI:

C1999-042562

TITLE:

New Streptococcus pneumoniae spoIIIE polypeptide and polynucleotide - useful as diagnostic reagents and for prevention and treatment of Streptococcal infections which cause bacteremia and meningitis.

DERWENT CLASS:

B04 D16

INVENTOR(S):

BROWN, J R; BRYANT, A P; CHALKER, A F; FELIU, M M

Z; ZALACAIN FELIU, M M

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (BROW-I) BROWN J R;

(BRYA-I) BRYANT A P; (CHAL-I) CHALKER A F; (FELI-I)

ZALACAIN FELIU M M

COUNTRY COUNT:

28

PATENT INFORMATION:

PATENT	NO	KIND	DATE	WEEK	LA	PG
EP 899	336	A2	19990303	(199913) *	FN	23

Shears 308-4994 Searcher :

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

US 5888770 A 19990330 (199920) CA 2241431 A 19990226 (199932)

JP 11225776 A 19990824 (199944) 60

US 6222016 B1 20010424 (200125)

US 2002019515 A1 20020214 (200214)

## APPLICATION DETAILS:

]	PA1	TENT NO	KIND			API	PLICATION	DATE
		899336 5888770	A2 A			 	1998-306605 1997-922837	19980818 19970826
(	CA	2241431	A			CA	1998-2241431	19980820
		11225776 6222016	A B1	Div	ev		1998-281887 1997-922837	19980826 19970826
,		0222010	DI	DIV	CA.	US	1999-351550	19990712
Ţ	JS	200201951	L5 A1				1997-922837	1997.0826
				Div	ex		1999-351550 2001-775978	19990712 20010202
						US	2001 113310	20010202

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
	B1 Div ex 15 A1 Div ex Div ex	US 5888770 US 5888770 US 6222016

PRIORITY APPLN. INFO: US 1997-922837 19970826; US 1999-351550 19990712; US 2001-775978 20010202

AN 1999-144807 [13] WPIDS

AB EP 899336 A UPAB: 19990331

A membrane bound protein (spoIIIE) involved in chromosome partitioning during sporulation and vegetative replication comprising at least 70% identity to sequence (I), a fully defined 783 amino acid protein given in the specification, is new. Also claimed are: (1) an isolated polynucleotide (II) (DNA or RNA) comprising a sequence selected from a polynucleotide which: (i) has 70% identity to a polynucleotide encoding: (a) polypeptide (I); (b) the mature spoIIIE polypeptide expressed by Streptococcus pneumoniae 0109933; (ii) is complementary to the polynucleotides; and (iii) comprises at least 15 sequential bases of polynucleotides (i) or (ii); (2) a vector comprising polynucleotide (II); (3) a host cell comprising the vector; (4) an antibody immunospecific to spoIIIE polypeptide (I); and (5) an antagonist which inhibits activity or expression of spoIIIE polypeptide (I).

USE - SPOIIIE polypeptides and polynucleotides are useful for diagnosing diseases due to an infection of an organism with the spoIIIE gene by detecting the presence of a spoIIIE encoding nucleic acid or analysing for the presence or amount of spoIIIE polypeptide (claimed). They can diagnose the stage and type of infection. SpoIIIE polypeptides are also useful for screening for compounds which affect activity of the protein by measuring the binding to polypeptide (I) and observing the stimulation or inhibition of the polypeptide function (claimed). These can be used in

treatment to inhibit (antagonist i.e. antibacterial drugs) or enhance (agonist) spoIIIE activity, in addition to direct administration of spoIIIE polypeptides to treat conditions associated with a lack of spoIIIE polypeptide (claimed), or direct administration of antisense sequences to prevent expression. SpoIIIE polypeptides (administered directly, in a vector and as a vaccine) and antibodies induce an immune response to immunise and prevent disease (claimed). Diseases diagnosed, prevented or treated include: bacterial infections, especially Streptococcus pneumoniae infections which cause otitis media, conjunctivitis, pneumonia, bacteremia, sinusitis, pleural empyema and endocarditis and especially meningitis. SpoIIIE polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection. Dwg.0/0

L22 ANSWER 33 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1999-123271 [11] WPIDS

DOC. NO. NON-CPI: N1999-090163

DOC. NO. CPI: C1999-036266

TITLE: New Streptococcus pneumoniae RNA polymerase alpha subunit (rpoA) polypeptide and polynucleotide -

useful as diagnostic reagents and for prevention and treatment of Streptococcus pneumoniae

infections which cause sinusitis and meningitis.

DERWENT CLASS: B04 D16 S03 INVENTOR(S): PALMER, L M

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP

COUNTRY COUNT: 27

PATENT INFORMATION:

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK

NL PT RO SE SI

CA 2239222 A 19990208 (199930)

JP 11206389 A 19990803 (199941) 56

## APPLICATION DETAILS:

PATENT NO F	KIND	APPLICATION	DATE
EP 896061	A2	EP 1998-306052	19980729
CA 2239222	A	CA 1998-2239222	19980731
JP 11206389	A	JP 1998-257430	19980807

PRIORITY APPLN. INFO: US 1997-907704 19970808

AN 1999-123271 [11] WPIDS

AB EP 896061 A UPAB: 19990316

A DNA-directed RNA polymerase alpha -subunit (rpoA) polypeptide comprising at least 70% identity to sequence (I), a fully defined 311 amino acid protein given in the specification is new. Also claimed are: (1) an isolated polynucleotide (II) (DNA or RNA)

comprising a sequence selected from a polynucleotide which: (i) has 70% identity to a polynucleotide encoding: (a) polypeptide (I); (b) the mature rpoA polypeptide expressed by Streptococcus pneumoniae 0100993; (ii) is complementary to the polynucleotides; and (iii) comprises at least 15 sequential bases of polynucleotides (i) or (ii); (2) a vector comprising polynucleotide (II); (3) a host cell comprising the vector; (4) an antibody immunospecific to rpoA polypeptide (I); and (5) an antagonist which inhibits activity or expression of rpoA polypeptide (I).

USE - RpoA polypeptides and polynucleotides are useful for diagnosing diseases related to over or underexpression of rpoA protein by identifying mutations in the rpoA gene, or determining rpoA polypeptide or mRNA expression levels due to an infection of an organism with the rpoA gene (claimed). They can diagnose the stage and type of infection. RpoA polypeptides are also useful for screening for compounds which affect activity of the protein by measuring the binding to polypeptide (I) and observing the stimulation or inhibition of the polypeptide function (claimed). These can be used in treatment to inhibit (antagonist i.e. antibacterial drugs) or enhance (agonist) rpoA activity, in addition to direct administration of rpoA polypeptides to treat conditions associated with a lack of rpoA polypeptide (claimed), or direct administration of antisense sequences to prevent expression. RpoA polypeptides (administered directly, in a vector and as a vaccine) and antibodies induce an immune response to immunise and prevent disease (claimed). Diseases diagnosed, prevented or treated include: bacterial infections, especially Streptococcus pneumoniae infections which cause otitis media, conjunctivitis, pneumonia, bacteremia, sinusitis, pleural empyema, endocarditis and particularly meningitis. RpoA polypeptides , polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection.

L22 ANSWER 34 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

1999-108351 [10] WPIDS

DOC. NO. CPI:

C1999-032524

TITLE:

New glycogen phosphorylase (GP) polypeptide and polynucleotide - useful as diagnostic reagents and for prevention and treatment of Streptococcus pneumoniae infections, including bacteremia and

meningitis.

DERWENT CLASS:

B04 D16

INVENTOR(S):

BURNHAM, M; BURNHAM, M K R

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC

COUNTRY COUNT:

28

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

EP 894861 A2 19990203 (199910)\* EN 40

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

US 5882885 A 19990316 (199918)

CA 2237045 A 19990117 (199927) JP 11137275 A 19990525 (199931) 8

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 894861	A2	EP 1998-305244	19980701
US 5882885	A	US 1997-896590	19970717
CA 2237045	Α	CA 1998-2237045	19980707
JP 11137275	A	JP 1998-236237	19980717

PRIORITY APPLN. INFO: US 1997-896590 19970717

AN 1999-108351 [10] WPIDS

AB EP 894861 A UPAB: 19990310

A glycogen phosphorylase (GP) polypeptide comprising at least 70% identity to sequence (I), a fully defined 752 amino acid protein given in the specification is new. Also claimed are: (1) an isolated polynucleotide (II) (DNA or RNA) comprising a sequence selected from a polynucleotide which: (i) has 70% identity to a polynucleotide encoding: (a) polypeptide (I); (b) the mature GP polypeptide expressed Streptococcus pneumoniae 0100993; (ii) is complementary to the polynucleotides; and (iii) comprises at least 15 sequential bases of polynucleotides (i) or (ii); (2) a vector comprising polynucleotide (II); (3) a host cell comprising the vector; (4) an antibody immunospecific to GP polypeptide (I); and (5) an antagonist which inhibits activity or expression of GP polypeptide (I).

GP polypeptides and polynucleotides are useful for diagnosing diseases related to over or underexpression of GP protein by identifying mutations in the GP gene, or determining GP polypeptide or mRNA expression levels due to an infection of an organism with the GP gene (claimed). They can diagnose the stage and type of infection. GP polypeptides are also useful for screening for compounds which affect activity of the protein by measuring the binding to polypeptide (I) and observing the stimulation or inhibition of the polypeptide function (claimed). These can be used in treatment to inhibit ( antagonist i.e. antibacterial drugs) or enhance (agonist) GP activity, in addition to direct administration of GP polypeptides to treat conditions associated with a lack of GP polypeptide (claimed), or direct administration of antisense sequences to prevent expression. GP polypeptides (administered directly, in a vector and as a vaccine) and antibodies induce an immune response to immunise and prevent disease (claimed). Diseases diagnosed, prevented or treated include: bacterial infections, especially Streptococcus pneumoniae infections, which cause otitis media, conjunctivitis, bacteremia, sinusitis, pleural empyema, endocarditis and especially meningitis. GP polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection.

L22 ANSWER 35 OF 49 WPIDS (C) 2002 THOMSON DERWENT ACCESSION NUMBER: 1999~108350 [10] WPIDS

DOC. NO. NON-CPI:

N1999-078433

DOC. NO. CPI:

C1999-032523

TITLE:

New Streptococcus pneumoniae prolyl tRNA synthetase (proS) polypeptide and polynucleotide - useful as

diagnostic reagents and for prevention and

treatment of Streptococcus pneumoniae infections,

including bacteremia and meningitis.

DERWENT CLASS:

B04 D16 S03

INVENTOR(S):

GENTRY, D R; GREENWOOD, R C; LAWLOR, E J

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP

COUNTRY COUNT:

PATENT INFORMATION:

PAT	ENT NO	) · K	IND	DA'	TE	W	EEK			LA	PC	3					
ED.	004050			10	00020		100	010									
EP	894858 R: AT												T.FT	мс	NIT.	DΨ	S F
,ΤP	110467								_		25	_	шо	110	1111		ОL
	200214										25	5					

#### APPLICATION DETAILS:

PATENT NO KIN	ND	APPLICATION	DATE
EP 894858 F JP 11046776 F JP 2002142782 F	A2 A A Div ex	EP 1997-308252 JP 1997-321883 JP 1997-321883 JP 2001-259873	19971017 19971017 19971017 19971017

PRIORITY APPLN. INFO: US 1997-902584 19970729

1999-108350 [10] WPIDS AN

AB 894858 A UPAB: 19990310

> A prolyl tRNA synthetase (proS) polypeptide comprising at least 70% identity to sequence (I), a fully defined 618 amino acid protein given in the specification is new. Also claimed are: (1) an isolated polynucleotide (II) (DNA or RNA) comprising a sequence selected from a polynucleotide which: (i) has 70% identity to a polynucleotide encoding: (a) polypeptide (I); (b) the mature proS polypeptide expressed Streptococcus pneumoniae 0100993; (ii) is complementary to the polynucleotides; and (iii) comprises at least 15 sequential bases of polynucleotides (i) or (ii); (2) a vector comprising polynucleotide (II); (3) a host cell comprising the vector; (4) an antibody immunospecific to proS polypeptide (I); and (5) an antagonist which inhibits activity or expression of proS polypeptide (I).

ProS polypeptides and polynucleotides are useful for diagnosing diseases related to over or underexpression of proS protein by identifying mutations in the proS gene, or determining proS polypeptide or mRNA expression levels due to an infection of an organism with the proS gene (claimed). They can diagnose the stage and type of infection. proS polypeptides are also useful for screening for compounds which affect activity of the protein by measuring the binding to polypeptide (I) and observing the stimulation or inhibition of the polypeptide function (claimed). These can be used in treatment to inhibit (antagonist i.e. antibacterial

drugs) or enhance (agonist) proS activity, in addition to direct administration of proS polypeptides to treat conditions associated with a lack of proS polypeptide (claimed), or direct administration of antisense sequences to prevent expression. proS polypeptides (administered directly, in a vector and as a vaccine) and antibodies induce an immune response to immunise and prevent disease (claimed). Diseases diagnosed, prevented or treated include: bacterial infections, especially Streptococcus pneumoniae infections, which cause otitis media, conjunctivitis, bacteremia, sinusitis, pleural empyema, endocarditis and especially meningitis. ProS polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection.

L22 ANSWER 36 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

1999-083576 [08] WPIDS

DOC. NO. CPI:

C1999-025353

TITLE:

New Histidine Kinase polypeptide and polynucleotide - useful as diagnostic reagents and for prevention

and treatment of Streptococcus pneumoniae

infections, especially meningitis.

DERWENT CLASS:

B04 D16

INVENTOR(S):

WALLIS, N G

B2 20020219 (200221)

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC; (WALL-I) WALLIS N G

COUNTRY COUNT:

PATENT INFORMATION:

PATENT NO	KIND DATE	WEEK	LA	PG		
EP 892059	A2 1999012	0 (199908	) * EN	37		
R: AL A	T BE CH CY DE	DK ES FI	FR GB G	GR IE IT	LI LT	LU LV MC MK
NL P	T RO SE SI					
CA 2235422	A 1998122	0 (199923	)			
JP 11123088	A 1999051	1 (199929	)	25		
US 20010067	99 A1 2001070	5 (200139	)			
US 6268172	B1 2001073	1 (200146	)			•

# US 6348340 B APPLICATION DETAILS:

PAT	ENT NO K	IND			API	PLICATION	DATE
EP	892059	A2			EP	1998-304782	19980617
CA	2235422	Α			CA	1998-2235422	19980618
JP	11123088	Α			JΡ	1998-210188	19980619
US	2001006799	Α1	Div	ex	US	1997-879941	19970620
					US	2000-747116	20001222
US	6268172	В1			US	1997-879941	19970620
US	6348340	В2	Div	ex	US	1997-879941	19970620
					US	2000-747116	20001222

## FILING DETAILS:

PATENT NO KIND

PATENT NO

US 6268172

US 6348340 B2 Div ex

PRIORITY APPLN. INFO: US 1997-879941 19970620; US 2000-747116

20001222

1999-083576 [08] WPIDS AN

ΑB 892059 A UPAB: 19990224

A Histidine Kinase (HK) polypeptide which is a component of the two component signal transduction system (TCSTS) in bacteria, comprising at least 70% identity to sequence (I), a fully defined 446 amino acid protein given in the specification is new. Also claimed are: (1) an isolated polynucleotide (II) (DNA or RNA) comprising a sequence selected from a polynucleotide which: (i) has 70% identity to a polynucleotide encoding: (a) polypeptide (I); (b) the mature HK polypeptide expressed Streptococcus pneumoniae 0100993; (ii) is complementary to the polynucleotides; and (iii) comprises at least 15 sequential bases of polynucleotides (i) or (ii); (2) a vector comprising polynucleotide (II); (3) a host cell comprising the vector; (4) an antibody immunospecific to HK polypeptide (I); and (5) an antagonist which inhibits activity or expression of HK polypeptide (I).

USE - HK polypeptides and polynucleotides are useful for diagnosing diseases related to over or underexpression of HK protein by identifying mutations in the HK gene, or determining HK polypeptide or mRNA expression levels due to an infection of an organism with the HK gene (claimed). They can diagnose the stage and type of infection. HK polypeptides are also useful for screening for compounds which affect activity of the protein by measuring the binding to polypeptide (I) and observing the stimulation or inhibition of the polypeptide function (claimed). These can be used in treatment to inhibit ( antagonist i.e. antibacterial drugs) or enhance (agonist) HK activity, in addition to direct administration of HK polypeptides to treat conditions associated with a lack of HK polypeptide (claimed), or direct administration of antisense sequences to prevent expression. HK polypeptides (administered directly, in a vector and as a vaccine) and antibodies induce an immune response to immunise and prevent disease (claimed). Diseases diagnosed, prevented or treated include: bacterial infections, especially Streptococcus pneumoniae infections, which cause otitis media, conjunctivitis, bacteremia, sinusitis, pleural empyema, endocarditis and especially meningitis. HK polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial

L22 ANSWER 37 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

infection.

1999-083519 [08] WPIDS

CROSS REFERENCE:

1999-037060 [04]; 2001-556618 [55]

DOC. NO. NON-CPI: DOC. NO. CPI:

N1999-060269 C1999-025296

TITLE:

New Streptococcus pneumoniae Response Regulator (RR) polypeptide and polynucleotide - useful as diagnostic reagents and for prevention and treatment of Streptococcus pneumoniae infections,

Shears 308-4994 Searcher :

including pleural empyema and meningitis.

DERWENT CLASS: INVENTOR(S):

B04 D16 S03 WALLIS, N G

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC; (WALL-I) WALLIS N G

COUNTRY COUNT:

28

PATENT INFORMATION:

PATENT NO	KIND DATE	WEEK	LA	PG		
EP 891984	A2 199901	20 (199908	 ) * EN	39		•
R: AL A	AT BE CH CY D	E DK ES FI	FR GB G	GR IE IT	LI LT	LU LV MC MK
NL E	T RO SE SI					•
CA 2235441	A 199812	20 (199923	)			
JP 11225772	2 A 199908	24 (199944	)	85		
	B1 200105					•
US 20020653	395 Al 200205	30 (200240	)			

## APPLICATION DETAILS:

PATENT NO K	IND	APPLICATION	DATE
EP 891984	A2	EP 1998-304786	19980617
CA 2235441	A	CA 1998-2235441	19980618
JP 11225772	A	JP 1998-210192	19980618
US 6224869	B1 Div ex	US 1997-879531	19970620
		US 1999-321276	19990527
US 2002065395	Al Div ex	US 1997-879531	19970620
		US 2001-800396	20010306

PRIORITY APPLN. INFO: US 1997-879531 19970620; US 1999-321276 19990527; US 2001-800396 20010306

AN 1999-083519 [08] WPIDS

CR 1999-037060 [04]; 2001-556618 [55]

AB EP 891984 A UPAB: 20020626

A Response Regulator (RR) polypeptide which is a component of the two component signal transduction system (TCSTS) in bacteria, comprising at least 70% identity to sequence (I), a fully defined 245 amino acid protein given in the specification is new. Also claimed are: (1) an isolated polynucleotide (II) (DNA or RNA) comprising a sequence selected from a polynucleotide which: (i) has 70% identity to a polynucleotide encoding: (a) polypeptide (I); (b) the mature RR polypeptide expressed by Streptococcus pneumoniae 0100993; (ii) is complementary to the polynucleotides; and (iii) comprises at least 15 sequential bases of polynucleotides (i) or (ii); (2) a vector comprising polynucleotide (II); (3) a host cell comprising the vector; (4) an antibody immunospecific to RR polypeptide (I); and (5) an antagonist which inhibits activity or expression of RR polypeptide (I).

RR polypeptides and polynucleotides are useful for diagnosing diseases related to over or underexpression of RR protein by identifying mutations in the RR gene, or determining RR polypeptide or mRNA expression levels due to an infection of an organism with the RR gene (claimed). They can diagnose the stage and type of infection. RR polypeptides are also useful for screening for compounds which affect activity of the protein by measuring the binding to

polypeptide (I) and observing the stimulation or inhibition of the polypeptide function (claimed). These can be used in treatment to inhibit ( antagonist i.e. antibacterial drugs) or enhance (agonist) RR activity, in addition to direct administration of RR polypeptides to treat conditions associated with a lack of RR polypeptide (claimed), or direct administration of antisense sequences to prevent expression. RR polypeptides (administered directly, in a vector and as a vaccine) and antibodies induce an immune response to immunise and prevent disease (claimed). Diseases diagnosed, prevented or treated include: bacterial infections, especially Streptococcus pneumoniae infections, which cause otitis media, conjunctivitis, bacteremia, sinusitis, pleural empyema, endocarditis and especially meningitis. RR polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection.

L22 ANSWER 38 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1999-072883 [07] WPIDS

CROSS REFERENCE: 1998-159452 [14]; 1998-458798 [40]; 1999-279570

[24]; 1999-347727 [29]

DOC. NO. CPI: C1

TITLE:

C1999-021868

New Streptococcus pneumoniae DNA helicase (PcrA)

polypeptide and polynucleotide - useful as diagnostic reagents and for prevention and

treatment of Streptococcus pneumoniae infections,

including meningitis.

DERWENT CLASS:

INVENTOR(S):

B04 D16

BLACK, M T; HODGSON, J E; HOLMES, D J; KNOWLES, D J

C; LONETTO, M A; NICHOLAS, R O; STODOLA, R K;

O'NICHOLAS, R

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

25

BEECHAM PLC

COUNTRY COUNT:

28

PATENT INFORMATION:

PATENT N	10 1	KIND	DATE	;	WEEK		I	ĹΑ	PC	3							
EP 89064	7	7.2	1000	0113	/100	9071	· *	יאי	3:	~ —							
			-		•												
R: A	L AT	ΒE	CH CY	DE	DK ES	FI	FR	GB	GR	ΙE	ΙT	LI	LT	LU	$rac{\Gamma}{\Lambda}$	MC	MK
N	L PT	RO	SE SI														
US 58587	18	Α	1999	0112	(199	910)	)										
CA 22364	73.	Α	1999	0108	(199	925)	)										

## APPLICATION DETAILS:

JP 11137271

PATENT NO	KIND	APPLICATION	DATE
EP 890647	A2	EP 1998-305343	19980706
		US 1997-889711	19970708
US 5858718	A	00 100 . 000 / 11	
CA 2236473	Α	CA 1998-2236473	19980706
JP 11137271	. A	JP 1998-229240	19980708

19990525 (199931)

PRIORITY APPLN. INFO: US 1997-889711 19970708 AN 1999-072883 [07] WPIDS 1998-159452 [14]; 1998-458798 [40]; 1999-279570 [24]; 1999-347727 CR [29] EΡ 890647 A UPAB: 20020730 AΒ A Streptococcal pneumoniae DNA helicase (PcrA) polypeptide comprising an amino acid sequence at least 70% identical to sequence (I), a fully defined 763 amino acid protein given in the specification is new. Also claimed are: (1) an isolated polynucleotide (DNA or RNA) sequence which: (i) is complementary or at least 70% identical to PcrA polynucleotide (II), a fully defined 2292 bp nucleic acid encoding (I); (ii) encodes a polypeptide complementary or at least 70% identical to (I); and (iii) comprises at least 15 sequential bases of (i) or (ii) (a probe); (2) a vector comprising polynucleotide of (1); (3) a host cell comprising the vector; (4) an antibody immunospecific for the PcrA polypeptide; and (5) an antagonist which inhibits activity or expression of the PcrA polypeptide. USE - PcrA polypeptides and polynucleotides are useful for diagnosing diseases related to over or underexpression of PcrA protein by identifying mutations in the PcrA gene using probes (1iii), or determining an increase in PcrA polypeptide expression levels due to an infection of an organism with the PcrA gene (claimed). PcrA polypeptides are useful for screening for compounds which affect activity of the protein by measuring the binding to polypeptide (I), and observing the stimulation or inhibition of polypeptide (I) function (claimed). These can be used for treatment to inhibit (antagonist i.e. antibacterial drugs) or enhance (agonist) PcrA activity, in addition to direct administration of PcrA polypeptides to treat conditions associated with a lack of PcrA polypeptide (claimed), or direct administration of antisense sequences to prevent expression. PcrA polypeptides (administered directly, in a vector and as a vaccine) and antibodies induce an immune response to immunise and prevent disease (claimed). Diseases diagnosed, prevented or treated include: bacterial infections, especially

otitis media; conjunctivitis; pneumonia; bacteremia; sinusitis; pleural empyema; endocarditis and especially meningitis. PcrA

proteins, and are useful for use on wounds and body implants

L22 ANSWER 39 OF 49 WPIDS (C) 2002 THOMSON DERWENT ACCESSION NUMBER: 1999-072877 [07] WPIDS

Streptococcus pneumoniae infections;

to prevent bacterial infection.

DOC. NO. CPI:

C1999-021862

polypeptides prevent adhesion of bacteria to matrix

TITLE:

New Streptococcus pneumoniae signal peptidase (II) (IspA) polypeptide and polynucleotide - useful as diagnostic reagents and for prevention and

the street of Characteristics infection

treatment of Streptococcus pneumoniae infections,

including meningitis.

DERWENT CLASS:

B04 D16

INVENTOR(S):

BLACK, M T; ODWYER, K M; O'DWYER, K M

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC

COUNTRY COUNT:

27

## PATENT INFORMATION:

#### APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE		
EP 890641	A1	EP 1998-305234	19980701		
CA 2236485	A	CA 1998-2236485	19980706		
JP 11127875	A	JP 1998-229900	19980710		

PRIORITY APPLN. INFO: US 1997-52215P 19970710

AN 1999-072877 [07] WPIDS

AB EP 890641 A UPAB: 19990217

A Streptococcus pneumoniae signal peptidase (II) (IspA) polypeptide comprising an amino acid sequence at least 70% identical to sequence (I), a fully defined 153 amino acid protein given in the specification is new. Also claimed are: (1) an isolated polynucleotide (DNA or RNA) sequence which: (a) is complementary or at least 70% identical to IspA polynucleotide (II), a fully defined 462 bp nucleic acid encoding (I); (b) encodes a polypeptide complementary or at least 70% identical to (I); and (c) comprises at least 15 sequential bases of (a) or (b) (a probe); (2) a vector comprising polynucleotide of (1); (3) a host cell comprising the vector; (4) an antibody immunospecific for the IspA polypeptide; and (5) an antagonist which inhibits activity or expression of the IspA polypeptide.

USE - IspA polypeptides and polynucleotides are useful for diagnosing diseases related to over or underexpression of IspA protein by identifying mutations in the IspA gene using probes (1c), or determining an increase in IspA polypeptide expression levels due to an infection of an organism with the IspA gene (claimed). IspA polypeptides are useful for screening for compounds which affect activity of the protein by measuring the binding to IspA polypeptide (I), and observing the stimulation or inhibition of polypeptide function (claimed). These can be used for treatment to inhibit (antagonist i.e. antibacterial drugs) or enhance (agonist) IspA activity, in addition to direct administration of IspA polypeptides to treat conditions associated with a lack of IspA polypeptide (claimed), or direct administration of antisense
sequences to prevent expression. IspA polypeptides (administered directly, in a vector and as a vaccine) and antibodies prevent disease induce an immune response to immunise an d (claimed). Diseases diagnosed, prevented or treated include: bacterial infections, especially Streptococcus pneumoniae infections; otitis media; conjunctivitis; pneumonia; bacteremia; sinusitis; pleural empyema; endocarditis and especially meningitis. IspA

polypeptides and polynucleotides prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection.

L22 ANSWER 40 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1999-062663 [06] WPIDS

DOC. NO. NON-CPI: N1999-046543 DOC. NO. CPI: C1999-018845

TITLE: New isolated gidA2 polypeptide from Streptococcus

pneumoniae - used to diagnose, treat and prevent bacterial infections e.g. S. pneumoniae and meningitis and H. pylori and related cancers,

ulcers and gastritis.

DERWENT CLASS: B04 D16 S03

INVENTOR(S): FEDON, J C; KALLENDER, H; LENOX, A L; PALMER, L M

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC

COUNTRY COUNT: 27

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

EP 889132 A2 19990107 (199906)\* EN 42 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK

NL PT RO SE SI

CA 2236441 A 19990101 (199924)

JP 11137266 A 19990525 (199931) 109

JP 2000050890 A 20000222 (200020) 37

# APPLICATION DETAILS:

PATENT NO K	IND .	·	API	PLICATION	DATE
EP 889132 CA 2236441 JP 11137266	A2 A A		CA	1998-305208 1998-2236441 1998-223539	19980630 19980629 19980701
JP 2000050890	A Div	ex		1998-223539 1999-212084	19980701 19980701

PRIORITY APPLN. INFO: US 1997-51378P 19970701

AN 1999-062663 [06] WPIDS

AB EP 889132 A UPAB: 19990217

New isolated polypeptide (I) is at least 70 % identical with sequences of 444 or 331 amino acids ((2) or (4) respectively) over the entire length, is or includes (2) or (4) or is encoded by recombinant nucleic acids of 1500 or 1195 base pairs ((1) and (3) respectively). Also claimed are: (i) an isolated nucleic acid (II) that encodes (I), is at least 70 % identical with (1) or (3), or other sequences encoding (2) and (4), over the entire length, is or includes (1) or (3), is obtained by screening a library with (1), (3) or their fragments under stringent conditions, encodes the mature polypeptide expressed by the gidA2 gene of Streptococcus pneumoniae or is complementary to any of the above in (i); (ii) an antibody (Ab) directed against (I); (iii) an agonist or antagonist (III) of the activity or expression of (I); (iv) an expression system for producing (I); (v) a host cell, or derived membranes, containing the above expression system; and (vi) a computer-readable

medium having sequence data for (I) and (II) stored on it. USE - (I), its agonists or (II) are used to treat conditions requiring increased activity or expression of (I), while conditions (particularly bacterial infections) requiring inhibition of such activity or expression are treated by administering an antagonist, inhibitory nucleic acid or competitive polypeptide Especially infection by S. pneumoniae (e.g. meningitis) is treated, but also H. pylori infections (and related cancers, ulcers and gastritis). These antibacterial agents may also be used to treat in-dwelling devices to prevent infection or generally as wound treatments to prevent adhesion of bacteria to matrix proteins. (I)-related conditions, or susceptibility to them, can be diagnosed, staged or prognosed by detecting mutations in (I)-encoding nucleic acid or by determining the presence or amount (I) or cell membranes of (v) are used to screen for (II) of (I). (in any standard binding assay) and cells of (v) are used to produce recombinant (I), used to raise Ab (for use in identifying/isolating (I)-expressing clones, for affinity purification, as therapeutic agent and in competitive drug screens), to identify (III) or specific receptors, in rational drug design and as immunogens for vaccines. (II) or its fragments are used as antisense/ribozyme therapeutics, as probes and primers to isolate homologous sequences, to detect (mutant) (II), for chromosomal mapping, to determine bacterial serotypes, for genetic immunisation, to screen for (III) and in rational drug design. The medium of (vi) is used to identify homologous sequences and in computer-based polynucleotide assembly (by detecting overlapping regions between different sequences). The active agents are administered e.g. topically, orally or by injection at a dosage of 0.01-10 (preferably 1) mg/kgand vaccinating doses of antigens are 0.5-5 mu g/kg, given 1-3 times at intervals of 1-3 weeks. Dwg.0/0

L22 ANSWER 41 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

1999-062661 [06] WPIDS

DOC. NO. NON-CPI:

N1999-046541

DOC. NO. CPI:

C1999-018843

TITLE:

New nucleic acid encoding gidB polypeptide from Streptococcus pneumoniae - used to diagnose, prevent and treat S. pneumoniae infections and meningitis and to prevent adhesion of bacteria to matrix proteins.

DERWENT CLASS:

B04 D16 S03

INVENTOR(S):

KALLENDER, H

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC

COUNTRY COUNT:

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

EP 889130 A2 19990107 (199906) \* EN 23

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK

NL PT RO SE SI

US 5866366 A 19990202 (199912)

28

CA	2236459	Α	19990101	(199924)	
JΡ	11137267	Α	19990525	(199931)	56
US	6207449	В1	20010327	(200119)	
US	6214346	В1	20010410	(200122)	•

# APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE			
EP 889130 US 5866366 CA 2236459	A2 A A	EP 1998-305183 US 1997-886633 CA 1998-2236459	19980630 19970701 19980630			
JP 11137267 US 6207449	A A B1 Div ex	JP 1998-223542 US 1997-886633	19980701 19970701			
US 6214346	B1 Div ex	US 1998-213081 US 1997-886633 US 1998-212979	19981216 19970701 19981216			

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 6207449	Bl Div ex	US 5866366
US 6214346	Bl Div ex	US 5866366

PRIORITY APPLN. INFO: US 1997-886633 19970701; US 1998-213081 19981216; US 1998-212979 19981216

AN 1999-062661 [06] WPIDS

AB EP 889130 A UPAB: 19990210

New isolated nucleic acid (I) is at least 70 % identical with a sequence encoding a 237 amino acid protein (2), is at least 70 % identical with a sequence encoding the mature polypeptide expressed by the gidB gene of Streptococcus pneumoniae 0100993 (NCIMB 40794), encodes a polypeptide at least 70 % identical with (2) and is the complement of or contains at least 15 sequential bases of any of the above. Also claimed are: (i) vectors containing (I); (ii) host cells containing this vector; (iii) polypeptides (II) at least 70 % identical with (2); (iv) antibodies (Ab) against (II); and (v) antagonists (III) that inhibit activity or expression of (II).

USE - Cells of (ii) are used to produce recombinant (II) or its fragments, used to screen for specific binding agents that inhibit or activate it (in standard binding assays), in vaccines to induce an immune (antibody and/or T cell) response (optionally expressed in vivo from a gene therapy vector) and to raise Ab (used to identify and isolate (II)-expressing clones, for affinity purification, as therapeutic inhibitors and in competitive drug screens or diagnostic immunoassays). (II) are used to treat conditions that require gidB polypeptide while (III) are used to treat conditions requiring inhibition of gidB, particularly bacterial infection. Particularly infections caused by S. pneumoniae (specifically meningitis) are treated, but the antibacterial agents may also be used to treat in-dwelling devices to prevent infection, or generally for wound treatment to prevent adhesion of bacteria to matrix proteins. (II)-related diseases are diagnosed by detecting mutations in (II)-en coding nucleic acid or by determining the

amount or presence of (II). Fragments of (I) are used for genetic immunisation, as probes and primers to isolate related sequences, for diagnosis and staging of infection (in standard hybridisation and amplification assays), for establishing bacterial serotype or genotype, in **drug** screening and as **therapeutic** antisense agents. The active agents are administered at a dosage of 0.01-10 (preferably 1) mg/kg e.g. by injection, topically, orally or from wound dressings. Doses of vaccinating antigen are 0.5-5 mu g/kg, using 1-3 doses at 1-3 week intervals.

L22 ANSWER 42 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1999-062659 [06] WPIDS

DOC. NO. NON-CPI: N1999-046539 DOC. NO. CPI: C1999-018841

TITLE: New isolated gidAl polypeptide from Streptococcus

pneumoniae - useful in diagnosis, treatment and

prevention of bacterial infections.

DERWENT CLASS: B04 D16 S03

INVENTOR(S): BURNHAM, M; FEDON, J C; JAWORSKI, D D; KALLENDER,

H; LENOX, A L; PALMER, L M; WANG, M

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC

COUNTRY COUNT: 28

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 889128	Ά2	19990107	(199906)*	EN	44

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

CA 2236425 A 19990101 (199924)

JP 11137268 A 19990525 (199931) 115

JP 2000210093 A 20000802 (200041) 40

US 6238882 B1 20010529 (200132)

## APPLICATION DETAILS:

PATENT NO K	IND	APPLICATION	DATE
EP 889128	A2	EP 1998-305174	19980630
CA 2236425	Α .	CA 1998-2236425	19980629
JP 11137268	A	JP 1998-223543	19980701
JP 2000210093	A Div ex	JP 1998-223543	19980701
		JP 2000-53626	19980701
US 6238882	B1 Provisional	US 1997-51379P	19970701
		US 1998-104068	19980624

PRIORITY APPLN. INFO: US 1997-51379P 19970701; US 1998-104068 19980624

AN 1999-062659 [06] WPIDS

AB EP 889128 A UPAB: 19990217

New isolated polypeptide (II) comprises/is (at least 70% identity to) sequence (2), 637 amino acids (aa) or (4) 623 aa, over their entire length and/or is encoded by a recombinant polynucleotide comprising sequence (1) 2100 bp or (3) 1871 bp (all sequences fully defined in the specification). Also claimed are: (A) an isolated

polynucleotide (I); (B) an antibody antigenic to or immunospecific for polypeptide (II); (C) a process for diagnosing or prognosing a (susceptibility to) disease in an individual related to expression or activity of (II); (D) a method for screening to identify compounds that activate or inhibit the function of (II); (E) an agonist/antagonist of the activity or expression of (II); (F) an expression system comprising (I) capable of producing (II) when present in compatible host cell; (G) a host cell comprising the above expression system/membrane expressing (II); (H) a process for producing (II) comprising culturing the host cell; (I) a process for producing the host cell comprising the expression system for (II); (J) a recombinant host cell capable of expressing (II); (K) a computer readable medium with stored sequences (1)-(4); and (L) a computer based method for performing homology identification.

USE - (I), its agonists or (II) are used to treat conditions requiring increased activity or expression of (I) (conditions not cited), while conditions (particularly bacterial infections) requiring inhibition of (I) are treated by administering an antagonist, inhibitory nucleic acid or competitive polypeptide e.g. S. pneumoniae infection, particularly meningitis and also Helicobacter pylori infections e.g. related cancers, ulcers and gastritis. These antibacterial agents may also be used to treat in-dwelling devices to prevent infection or generally as wound treatments to prevent adhesion of bacteria to matrix proteins. (I)-related conditions, or susceptibility to them, can be diagnosed, staged or prognosed by (i) detecting mutations in (I)-encoding nucleic acid or (ii) by determining presence or amount of (I). (I), or cell membranes of (E), are used to screen for (II) (in any standard binding assay) and cells of (E) are used to produce recombinant (I), used (i) to raise Ab (for use in identifying/isolating (I)-expressing clones, for affinity purification, as therapeutic agent and in competitive drug screens); (ii) to identify (III) or specific receptors; (iii) in rational drug design and (iv) as immunogen for vaccines. (II), or its fragments, are used as antisense/ribozyme therapeutics; as probes and primers to isolate homologous sequences; to detect (mutant) (II); for chromosomal mapping; to determine bacterial serotype; for genetic immunisation; to screen for (III) and in rational drug design. Dwg.0/0

L22 ANSWER 43 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1999-047880 [05] WPIDS

DOC. NO. NON-CPI: N1999-035027
DOC. NO. CPI: C1999-015230

DOC. NO. CPI: C1999-015230
TITLE: New Streptoco

New Streptococcus pneumoniae Histidine Kinase polypeptide and polynucleotide - useful as diagnostic reagents and for prevention and

treatment of Streptococcus pneumoniae infections.

DERWENT CLASS: B04 D16 T01

INVENTOR(S): BISWAS, S; GE, J Y; HOLMES, D J; INGRAHAM, K A;

JAWORSKI, D D; SHILLING, L K; THROUP, J; WALLIS, N

G; WANG, M; ZALACAIN, M; GE, J; HOLMES, D;

INGRAHAM, K; JAWORSKI, D; SHILLING, L; WALLIS, N

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

#### BEECHAM PLC

COUNTRY COUNT:

27

PATENT INFORMATION:

PAT	rent	МО		KINI	) DI	ATE		WE	EEK		]	LA	PG	3							
EP	887	 413		A2	2 19	998:	1230	) (:	199	905)	) * ]	EN	43	3							
	R:	AL	ΑT	BE	CH	CY	DE	DK	ES	FI	FR	GB	GR	ΙE	ΙT	LI	LT	LU	$rac{r}{\Lambda}$	MC	MK
		NL	PΤ	RO	SE	SI															
CA	223	353	9	Α	19	998	1130	( )	199	920)	)										
.TP	110	758	7.8	Δ	1 9	999	1323	1	199	9221	١		112	)	•						

#### APPLICATION DETAILS:

PATENT NO F	KIND	APPLICATION	DATE
EP 887413	A2	EP 1998-304140	19980526
CA 2233539	A	CA 1998-2233539	19980528
JP 11075878	Α	JP 1998-188025	19980529

PRIORITY APPLN. INFO: US 1997-48078P 19970530

AN 1999-047880 [05] WPIDS

AB EP 887413 A UPAB: 19990203

A new Histidine Kinase (HK) which is a component of the two component signal transducer system (TCSTS) is selected from: (i) an isolated polypeptide comprising an amino acid sequence having at least 70-95% identity to sequence (I), and 70-99% identity to sequence (II), fully defined 324 and 235 amino acid proteins respectively, given in the specification; (ii) an isolated polypeptide comprising HK sequence (I) or (II); (iii) an isolated polypeptide which is HK sequence (I) or (II); and (iv) a polypeptide encoded by a recombinant polynucleotide comprising sequence (III) or (IV), fully defined 1500 and 800 bp nucleic acids given in the specification. Also claimed are: (1) an isolated polynucleotide complementary or at least 70-95% identical to sequences (III) or (IV) encoding HK polypeptide (I) or (II); (2) an expression system comprising HK polynucleotide (III) or (IV); (3) a host cell comprising expression system or a membrane of (2); (4) an antibody immunospecific for the HK polypeptide; (5) an agonist or antagonist of the HK polypeptide; (6) a method for the treatment of an individual: (i) needing enhanced activity/expression of HK polypeptide by administering: (a) agonist of (5); or (b) HK polynucleotide of (1) in vivo; or (ii) needing to inhibit activity/expression of the HK polypeptide by administering: (a) antagonist of (5); or (b) a nucleic acid molecule which inhibits expression of the HK polynucleotide; or (c) a polypeptide which competes with the HK polypeptide for its ligand, substrate or receptor; and (7) a computer readable medium stored with data selected from: (i) HK polynucleotides (III)/(IV) or polypeptides (I)/(II); (ii) a set of polynucleotides or polypeptides, where at least one sequence is an HK polynucleotide or polypeptide; and (iii) a data set representing HK polynucleotides or polypeptides.

USE - HK polynucleotides and **polypeptides** are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the HK gene or analysing for the presence or amount of HK **polypeptide** expressed in a patient sample (claimed). HK PCR probes are useful for diagnosing diseases, and can

characterise the stage and the species or strain causing the infection. HK probes can also determine the response of the infectious organism to drugs. HK polypeptides and polynucleotides are useful for screening for antagonists , agonists and drugs against infectious micro-organisms. HK agonists and antagonists are bacteriostatic and bacteriocidal compounds which can be used in treatment to enhance (agonist) or block (antagonist or antisense sequence) HK activity, therefore treating bacterial infections, especially infections caused by Streptococcus pneumoniae. Epitopes of HK polypeptides and polynucleotides are useful immunogens for producing anti-HK antibodies for prevention of bacterial infections, and HK polynucleotides can be used in genetic immunisation (gene therapy) to prevent infections. HK polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection. HK polypeptides and polynucleotides may also be used as reagents for differential screening methods e.g. using probes in RT-PCR to identify and quantify genes expressed in bacterial tissue. HK polypeptides are useful for mapping the genes to chromosomes, allowing gene inheritance to be studied through linkage analysis. The computer based method (7) is useful for performing homology identification by comparing a polynucleotide with HK sequences (7), and is also useful for polynucleotide assembly, by screening for overlapping sequences between a polynucleotide and HK polynucleotides (III) or (IV) (claimed).

WPIDS (C) 2002 THOMSON DERWENT L22 ANSWER 44 OF 49 1999-047878 [05] WPIDS ACCESSION NUMBER:

N1999-035025 DOC. NO. NON-CPI:

DOC. NO. CPI: C1999-015228

TITLE: New Streptococcus pneumoniae N-acetylglucosamine-1phosphate uridyltransferase (GlmU) polypeptides and polynucleotides - useful as diagnostic reagents and for prevention and treatment of Streptococcal and

Heliobacter pylori infections.

B04 D16 S03 DERWENT CLASS:

DEBOUCK, C M; JAWORSKI, D D; MOONEY, J L; SHILLING, INVENTOR(S):

L K; WALLIS, N G; WANG, M; ZHONG, Y Y; DEBOUCK, C

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE PATENT ASSIGNEE(S):

BEECHAM PLC

COUNTRY COUNT: PATENT INFORMATION:

28

PG PATENT NO KIND DATE WEEK LA

A2 19981230 (199905)\* EN EP 887411 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK

NL PT RO SE SI

A 19981226 (199923) CA 2235778

JP 11155582 A 19990615 (199934) 62

A 20000328 (200023) US 6043071 US 6204042 B1 20010320 (200118)

APPLICATION DETAILS:

308-4994 Searcher Shears

PATENT NO	KIND	APPLICATION	DATE
EP 887411 CA 2235778	A2 A	EP 1998-304819 CA 1998-2235778	19980618 19980625
JP 11155582	A	JP 1998-218453	19980625
US 6043071	A Provisional	US 1997-50996P	19970626
		US 1997-971782	19971117
US 6204042	B1 Provisional	US 1997-50996P	19970626
	Div ex	US 1997-971782	19971117
		US 1999-309026	19990510

#### FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 6204042	B1 Div ex	US 6043071

PRIORITY APPLN. INFO: US 1997-971782 19971117; US 1997-50996P 19970626; US 1999-309026 19990510

AN 1999-047878 [05] WPIDS

AB EP 887411 A UPAB: 19990203

An N-acetylglucosamine-1-phosphate uridyltransferase (GlmU) polypeptide comprising an amino acid sequence at least 70% identical to sequence (I), a fully defined 459 amino acid protein given in the specification is new. Also claimed are: (1) an isolated polynucleotide (II) (DNA or RNA) comprising a polynucleotide with at least 70% identity to a nucleotide sequence encoding (I); (2) a vector comprising polynucleotide (II); (3) a host cell comprising the vector; (4) an antibody immunospecific for GlmU polypeptide (I); (5) an antagonist of GlmU polypeptide (I); and (6) an isolated polynucleotide (IV) comprising a polynucleotide with at least 70% identity to sequence encoding polypeptide (III), a fully defined 380 amino acid protein given in the specification.

USE - GlmU polypeptides and polynucleotides are useful for diagnosing diseases related to over or underexpression of the GlmU protein by identifying mutations in the GlmU gene, or analysing for the presence or amount of GlmU polypeptide in an individual, due to an infection of an organism with the GlmU gene (claimed), preferably humans infected with Streptococcus pneumoniae. GlmU polypeptides are also useful for screening for compounds which affect activity of the protein (claimed). These can be used for treatment to inhibit (antagonist i.e. antibacterial drugs) or enhance (agonist or GlmU polypeptide) GlmU activity (claimed), and are useful for treating microbial infections, especially Streptococcus pneumoniae infections which cause otitis media, conjunctivitis, pneumonia, bacteremia, meningitis, sinusitis, pleural empyema and endocarditis, and Heliobacter pylori induced cancers and infections, and can cure gastric ulcers and gastritis. GlmU polypeptide epitopes (administered directly, in a vector or as a vaccine) are useful for inoculating against infections by inducing a T cell and/or antibody response to protect against disease (claimed), especially against Streptococcus pneumoniae bacteria. Antibodies can also be administered to immunise and protect against disease. GlmU polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of

bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection.

L22 ANSWER 45 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

1999-037019 [04] WPIDS

DOC. NO. NON-CPI:

N1999-027917

DOC. NO. CPI:

C1999-011265

TITLE:

New Streptococcus pneumoniae response regulator

polypeptide and polynucleotide - useful as diagnostic reagents and for prevention and

treatment of Streptococcus pneumoniae infections.

DERWENT CLASS:

BO4 D16 S03 BISWAS, S; THROUP, J; WALLIS, N G; ZALACAIN, M

INVENTOR(S):
PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC

COUNTRY COUNT:

28

PATENT INFORMATION:

PATENT NO	KIND DATE	WEEK	LA	PG

EP 885902 A2 19981223 (199904) \* EN 43

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK

NL PT RO SE SI

CA 2235442 A 19981220 (199923)

JP 11137262 A 19990525 (199931) 36

US 6140061 A 20001031 (200057)

## APPLICATION DETAILS:

PATENT NO	KIND		API	PLICATION	DATE
EP 885902 CA 2235442 JP 11137262 US 6140061	A2 A A A	Provisional	CA JP US	1998-304775 1998-2235442 1998-210190 1997-50332P 1998-94103	19980617 19980618 19980618 19970620 19980609

PRIORITY APPLN. INFO: US 1997-50332P 19970620; US 1998-94103 19980609

AN 1999-037019 [04] WPIDS

AB EP 885902 A UPAB: 19990127

A new response regulator (RR) polypeptide which is a component of the two component signal transducer system (TCSTS) is selected from: (i) an isolated polypeptide comprising an amino acid sequence having at least 70-95% identity to sequence (I), and 70-99% identity to sequence (II), fully defined 232 and 208 amino acid proteins respectively, given in the specification; (ii) an isolated polypeptide comprising RR sequence (I) or (II); (iii) an isolated polypeptide which is RR sequence (I) or (II); and (iv) a polypeptide encoded by a recombinant polynucleotide comprising sequence (III) or (IV), fully defined 1172 and 1100 bp nucleic acids respectively, given in the specification. Also claimed are: (1) an isolated polynucleotide complementary or at least 70-95% identical to sequences (III) or (IV) encoding RR polypeptide (I) or (II); (2) an expression system comprising RR polynucleotide (III) or (IV); (3) a host cell comprising expression system or a membrane of (2); (4) an antibody immunospecific for the RR polypeptide; (5) an agonist or

antagonist of the RR polypeptide; (6) a method for the treatment of an individual: (i) needing enhanced activity/expression of RR polypeptide by administering: (a) agonist (5); or (b) RR polynucleotide (1) in vivo; or (ii) needing to inhibit activity/expression of the RR polypeptide by administering (a) antagonist (5); or (b) a nucleic acid molecule which inhibits expression of the RR polynucleotide; or (c) a polypeptide which competes with the RR polypeptide for its ligand, substrate or receptor; and (7) a computer readable medium stored with data selected from: (i) RR polynucleotides (III)/(IV) or polypeptides (I)/(II); (ii) a set of polynucleotides or polypeptides, where at least one sequence is an RR polynucleotide or polypeptide; and (iii) a data set representing RR polynucleotides or polypeptides.

USE - RR polynucleotides and polypeptides are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms in the RR gene or analysing for the presence or amount of RR polypeptide expressed in a patient sample (claimed). RR PCR probes are useful for diagnosing diseases, and can characterise the stage and the species or strain causing the infection. The RR probes can also determine the response of the infectious organism to drugs. RR polypeptides and polynucleotides are useful for screening for antagonists , agonists and drugs against infectious micro-organisms. RR agonists and antagonists are bacteriostatic and bacteriocidal compounds which can be used in treatment to enhance (agonist) or block (antagonist or antisense sequence) RR activity, therefore treating bacterial infections, especially infections caused by Streptococcus pneumoniae. Epitopes of RR polypeptides and polynucleotides are useful immunogens for producing anti-RR antibodies for prevention of bacterial infections, and RR polynucleotides can be used in genetic immunisation (gene therapy) to prevent infections. RR polypeptides, polynucleotides and their (ant)agonists can prevent adhesion of bacteria to matrix proteins, and are useful for use on wounds and body implants to prevent bacterial infection. RR polypeptides and polynucleotides may also be used as reagents for differential screening methods e.g. using probes in RT-PCR to identify and quantify genes expressed in bacterial tissue. RR polypeptides are useful for mapping genes to chromosomes, allowing gene inheritance to be studied through linkage analysis. The computer based method (7) is useful for performing homology identification by comparing a polynucleotide with RR sequences (7), and is also useful for polynucleotide assembly, by screening for overlapping sequences between a polynucleotide and RR polynucleotides (6) (claimed).

WPIDS (C) 2002 THOMSON DERWENT L22 ANSWER 46 OF 49

ACCESSION NUMBER: 1999-011652 [02] WPIDS

DOC. NO. NON-CPI: N1999-008769 DOC. NO. CPI:

TITLE:

C1999-004013

New isolated nucleic acid encoding rnc protein of

Streptococcus pneumoniae - and related vectors,

transformants, antibodies, proteins, and antagonists, for treatment, prevention and

diagnosis of infections.

DERWENT CLASS:

B04 D16 S03

INVENTOR(S):

LONETTO, M; ROSENBERG, M; LONETTO, M A

308-4994 Searcher : Shears

55

MK

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

BEECHAM PLC

COUNTRY COUNT: 28

PATENT INFORMATION:

PAT	ENT	ИО	F	KINI	D DA	ATE		WI	EEK		]	LA '	P	3							
<del>-</del>																					
	882																				
	R:	AL	ΑT	BE	CH	CY	DE	DK	ES	FI	FR	GB	GR	ΙE	IT	LI	LT	LU	$r_{\Lambda}$	MC	ľ
		NL	PΤ	RO	SE	SI															
TIC	586	6369	5	Δ	1 (	1000	1202	2 1	199	912	١										

US 5866365 A 19990202 (199912) CA 2233591 A 19981205 (199920) JP 11103870 A 19990420 (199926)

US 6251630 B1 20010626 (200138)

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 882796 US 5866365 CA 2233591 JP 11103870 US 6251630	A2 A A A B1 Div ex	EP 1998-304320 US 1997-869674 CA 1998-2233591 JP 1998-193551 US 1997-869674	19980601 19970605 19980602 19980603 19970605
*		US 1998-213010	19981216

## FILING DETAILS:

PATENT	NO F	KIND			PA	CENT	NO	
								-
US 6253	1630	В1	Div	ex	US	5866	365	

PRIORITY APPLN. INFO: US 1997-869674 19970605; US 1998-213010 19981216

AN 1999-011652 [02] WPIDS

AB EP 882796 A UPAB: 19990113

New isolated nucleic acid (I) is claimed which has (a) has at least 70% identity with a sequence encoding a 232 amino acid (aa) polypeptide (2), given in the specification, or with a sequence at least 70% identical with a sequence encoding the mature polypeptide for the rnc protein (a ribonuclease III family member) of Streptococcus pneumoniae 0100993 (NCIMB 40794); (b) encodes a polypeptide (2a) at least 70% identical with (2); (c) is the complement of (a) or (b); or (d) includes at least 15 sequential bases from (a) or (b).

Also new are (A) vectors containing (I); (B) host cells containing such vectors; (C) polypeptide (II) at least 70% identical with (2); (D) antibodies (Ab) against (II) and (E) antagonists of (II).

USE - Cells of (B) are used to express (II) which is useful therapeutically; to screen for compounds that interact with, and activate or inhibit, it (potential antibacterial agents) and to generate Ab (including as vaccines to provide a protective response, and in this case (II) may be expressed in vivo from (I)).

(II) and its agonists are used to **treat** conditions where rnc **polypeptide** is required (no examples) and the **antagonists** where rnc **polypeptide** needs to be **inhibited**, particularly a wide range of **infections** 

caused by **S. pneumoniae**, most particularly meningitis. (II) also **inhibit** adhesion of bacteria to extracellular matrix **proteins**, in-dwelling devices and wound surfaces.

Diseases associated with expression of (II) are diagnosed (a) by analysing a sample for presence of (II) or (b) by detecting nucleic acid encoding (II).

Ab are useful as antibacterial agents; to isolate or identify (II)-expressing clones and for affinity purification.

Fragments of (I) are useful as probes or primers to isolate full-length or related sequences; to screen for **drugs**, and to diagnose or stage infections, also for genotyping and serotyping of infective agents (e.g. by detecting mutations).

Therapeutic agents are administered by injection, topically, orally etc., generally at 0.01-10, usually about 1, mg/kg. To inhibit bacterial adhesion, a solution containing 0.001-10 mg/ml is applied to the catheter or other surface to be treated, and vaccines are administered at 0.5-5 mu g/kg, 1-3 times at 1-3 week intervals. Dwg.0/0

L22 ANSWER 47 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1999-001398 [01] WPIDS

DOC. NO. NON-CPI: N1999-001241
DOC. NO. CPI: C1999-000468

TITLE: New Streptococcus pneumoniae peptide releasing

factor polypeptide and polynucleotide - useful as

diagnostic reagents and for prevention and treatment of diseases caused by bacterial

infections, including meningitis and pneumonia.

DERWENT CLASS: B04 D16 S03 INVENTOR(S): PEARSON, S C

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP

COUNTRY COUNT: 28

PATENT INFORMATION:

PAT	TENT NO	KIND	DATE	WEEK	LA	PG							
EP	881292		1998120	2 (199901	) * EN	27.							
D.,				DK ES FI	•		IT	LI	LT	LU	LV	MC I	MK
	NL PT	RO S	SE SI										
CA	2233561	Α	1998112	9 (199920	)								
JΡ	11123087	Α	1999051	1 (199929	)	61							
US	5919664	Α	1999070	6 (199933	)								
ΠS	6372487	<b>R</b> 1	2002041	6 (200232	<b>Y</b>								

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 881292 CA 2233561 JP 11123087 US 5919664 US 6372487	A2 A A A B1 Div ex	EP 1998-304157 CA 1998-2233561 JP 1998-188019 US 1997-865311 US 1997-865311	19980526 19980527 19980529 19970529 19970529
		US 1999-315720	19990520

## FILING DETAILS:

PATENT NO KIND PATENT NO
US 6372487 B1 Div ex US 5919664

PRIORITY APPLN. INFO: US 1997-865311 19970529; US 1999-315720 19990520

AN 1999-001398 [01] WPIDS

AB EP 881292 A UPAB: 19990113

A Streptococcus pneumoniae peptide releasing factor (prfC) polypeptide comprising an amino acid sequence which is least 70% identical to sequence (I), a fully defined 515 amino acid protein given in the specification is new. Also claimed are: an isolated polynucleotide (II) (DNA or RNA) selected from a polynucleotide sequence which: (a) encodes above prfC polypeptide; (b) has at least 70% identity to a polynucleotide encoding prfC polypeptide (I); (c) has at least 70% identity to the prfC gene of Streptococcus pneumoniae 0100993 strain; (d) is complementary to (a), (b) or (c); and (e) comprises at least 15 sequential bases of polynucleotide (I); (2) a vector comprising prfC polynucleotides; (3) a host cell comprising vector of (2); (4) an antibody immunospecific for prfC polypeptides; (5) an antagonist of prfC polypeptides; and (6) a method for identifying compounds which interact and inhibit or activate prfC polypeptides.

USE - PrfC polypeptides and polynucleotides are useful for diagnosing susceptibility to diseases by detecting mutations or polymorphisms of the prfC gene. PCR using prfC probes is useful for diagnosing diseases caused by organisms comprising the prfC gene by detection at the nucleic acid level, and analysing for the presence or amount of prfC polypeptide (I) (claimed) in cell or tissue samples. This method is useful for diagnosing the stage of infection and the type of pathogen. PrfC polypeptides and polynucleotides can be used to screen for antagonists (claimed) and agonists (especially bacteriostatic and bacteriocidal compounds), which can be used in treatment to enhance (polypeptide (I)) or block ( antagonist) prfC activity (claimed). Polypeptide (I) is useful for screening for antibacterial compounds which can be used as drugs. PrfC polynucleotides can be used in genetic immunisation (gene therapy) to protect against bacterial infections. An immunological response can be induced by administering prfC polypeptide (I) or an antigenic fragment i.e. a vaccine, or nucleic acid vectors which direct expression of prfC protein or protein fragment in vivo, to induce an antibody and/or T cell immune response to protect against disease (claimed). This method is especially useful for preventing bacterial infections (especially Streptococcus pneumoniae) caused by surgical implants e.g. pacemakers, and the implant may also be bathed in prfC polypeptide (I) prior to insertion. PrfC polypeptides, polynucleotides and antagonists may be used as a wound treatment to prevent adhesion of bacteria to matrix proteins, as they interfere with the physical interaction between the pathogen and mammalian host. PrfC antibodies are also useful for inducing an immune response to immunise and prevent disease, and for isolating prfC clones or purifying the peptide by affinity chromatography. Diseases diagnosed, prevented or treated include: otits media, conjunctivitis, pneumonia, bacteremia,

sinusitis, pleural empyema, endocarditis and especially meningitis.

L22 ANSWER 48 OF 49 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

1997-549678 [50] WPIDS

DOC. NO. CPI:

C1997-175317

TITLE:

Response regulator or histidine kinase of

Streptococcus pneumoniae NCIMB 40794 - useful for treatment, prevention, and diagnosis of infection,

especially meningitis.

DERWENT CLASS:

B04 D16

INVENTOR(S):

WALLIS, N G

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE

57

SE

BEECHAM PLC

COUNTRY COUNT:

20

PATENT INFORMATION:

PAT	ENT	NO	,	KINT	נט נ	ATE.		WE	LEK			LΑ	P	3			
WO	974:	 1146	5 5	<b>-</b> A1	. 19	9971	1106	5 (1	199	750)	* ]	EN	4	 7			
	RW:	ΑT	BE	CH	DE	DK	ES	FI	FR	GB	GR	ΙE	ΙT	LU	MC	NL	PT
	W:	JP	US														

EP 954525 A1 19991110 (199952) EN

R: BE CH DE DK FR GB IT LI NL

JP 2000509984 W 20000808 (200043)

US 6217861 B1 20010417 (200123)

## APPLICATION DETAILS:

PATENT NO KI	IND	APPLICATION	DATE
WO 9741146	A1	WO 1997-US7375	19970501
EP 954525	A1	EP 1997-926395	19970501
		WO 1997-US7375	19970501
JP 2000509984	W	JP 1997-539234	19970501
		WO 1997-US7375	19970501
US 6217861	B1 Div ex	US 1997-850116	19970501
		US 1999-342461	19990629

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 954525	Al Based on 84 W Based on	WO 9741146 WO 9741146

PRIORITY APPLN. INFO: GB 1996-9122 19960501; GB 1996-9023

19960501

AN 1997-549678 [50] WPIDS

AB WO 9741146 A UPAB: 19971217

A novel nucleic acid sequence (I) is selected from: (a) a polynucleotide with at least 70% identity with a sequence encoding 217, 117 or 174 amino acid (aa) sequences given in the specification, or is their complement; (b) has at least 70% identity with a sequence encoding the same mature polypeptide as that expressed by the response regulator (RR) or histidine kinase (HK) gene of Streptococcus pneumoniae 0100993 (NCIMB 40794) or (c) contains at least 15 sequential bases of (a) or (b). Also new are: (1) a vector containing (I); (2) a host cell containing the vector

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of (1); (3) a polypeptide (A) at least 70% identical to the 217, 117
   or 174 aa sequences; (4) an antibody (Ab) against (A); (5) an
   antagonist (B) that inhibits the activity or expression of (A); (6)
    a method for the diagnosis of a disease related to the
    expression or activity of (A), by determining the sequence of the
    nucleic acid encoding it or analysing for the presence or amount of
    (A); and (7) a method for identifying compounds that
    interact with, and inhibit or activate, (A).
         USE - (I) is used to produce recombinant (A) or their
    fragments. (A) is used to treat conditions requiring the
    RR or HK polypeptide, while conditions requiring
    inhibition of RR or HK are treated with (B),
    particularly those that are antibacterial, preferably for
    treating S. pneumoniae infection
    , specifically meningitis (all claimed). (I) can also be used as a
    probe or primer to isolate related nucleic acid sequences (e.g.
    full-length clones), for diagnosis or staging of infection, to
    detect mutations and polymorphisms in the RR gene, to identify S.
    pneumoniae, to develop antibacterials and to express antisense
    nucleic acids. (I), or its fragments encoding non-variable regions
    of a bacterial cell surface protein, can be used in animal
    models of infection to determine immunologically active epitopes for
    subsequent production of therapeutic monoclonal
    antibodies. (A) are also used to identify (B) and to generate Ab
    (useful as (B) or as immunoassay reagents). (I), (A), and (B) may al
    so be used to inhibit adhesion of bacteria to
    extracellular matrix in/on e.g. wound surfaces or in-dwelling
    devices such as prostheses (which can be soaked in a solution of (B)
    before implanting).
     Dwg.0/0
                      WPIDS (C) 2002 THOMSON DERWENT
L22 ANSWER 49 OF 49
                                         WPIDS
                      1997-526211 [48]
                      C1997-167367
DOC. NO. CPI:
```

B04 D16

ACCESSION NUMBER:

TITLE:

New isolated nucleic acid encoding glutamyl tRNA synthetase of Streptococcus pneumoniae - useful for diagnosis, treatment and prevention of bacterial

infections, especially meningitis.

DERWENT CLASS:

INVENTOR(S):

LAWLOR, E J; JAWORSKI, D D; WANG, M

PATENT ASSIGNEE(S):

(SMIK) SMITHKLINE BEECHAM CORP; (SMIK) SMITHKLINE BEECHAM PLC; (JAWO-I) JAWORSKI D D; (LAWL-I) LAWLOR

E J; (WANG-I) WANG M

20 COUNTRY COUNT:

PATENT INFORMATION:

PATEN	IT NO	KIND	DATE	WEEK	LA	PG				
WO 9	738718 7: AT B	A1 SE CH I	19971 DE DK	023 (199748) ES FI FR GB	* EN GR IE	42 IT LU	MC	NL	РТ	SE
EP 90	V: JP U 04103 R: BE C	IS A1 CH DE	19990 DK FR	331 (199917) GB IT LI NL	EN	50				
	)005092 165760	261 W A	20000 20001	725 (200041) 226 (200103)	) )	50				

B1 20011009 (200162)

# APPLICATION DETAILS:

US 6300119

308-4994 Shears Searcher :

PA:	TENT NO K	IND			API	PLICATION	DATE
	9738718 904103	A1 A1			EP	1997-US6753 1997-918782 1997-US6753	19970418 19970418 19970418
JP	2000509261	W			JP	1997-056753 1997-537438 1997-US6753	19970418 19970418
US	6165760	Α	CIP Div	-	US	1997-844153 1997-962203 1999-282125	19970418 19971031 19990331
US	6300119	B1	CIP Div		US	1997-844153 1997-962203 1999-273142	19970418 19971031 19990319

## FILING DETAILS:

PATENT NO KIND PATENT NO					
EP 904103 JP 2000509261	Al Based on	WO 9738718 WO 9738718			
US 6165760	A CIP of	US 5958734			
US 6300119	Div ex B1 CIP of	US 5976840 US 5958734			
•	Div ex	US 5976840			

PRIORITY APPLN. INFO: GB 1996-7992 19960418

AN 1997-526211 [48] WPIDS

AB WO 9738718 A UPAB: 19971209

New isolated nucleic acid (I) is defined as follows: (a) has at least 70% identity to sequences encoding peptides (2), (4) or (6) of 348,126 and 62 amino acids (aa), respectively, reproduced in the specification; (b) is the complement of (a); (c) has at least 70% identity to a sequence encoding the same mature polypeptide expressed by the gluS gene (encoding glutamyl tRNA synthetase) in Streptococcus pneumoniae 0100993 (NCIMB 40794); (d) includes at least 15 sequential bases of (a)-(c). Also new are : (i) vectors containing (I); (ii) host cells containing this vector; (iii) polypeptides (II) at least 70% identical with (2), (4) or (6); (iv) antibodies (Ab) against (II); (v) antagonists (III) of the activity or expression of (II); (vi) diagnosis of disease related to expression/activity of (II) by sequencing (I) and/or analysing for presence or concentration of (II); (vii) method for identifying compounds (IV) that interact with, and inhibit or activaté, (II).

USE - (I) are used to express recombinant (II), i.e. the gluS polypeptide or their fragments, which are used to treat conditions that require gluS activity, also as antisense sequences to control expression of (II). (II), or vectors that express them, are used to induce an immune (antibody and/or T cell) response, specifically for protection against S. pneumoniae infection or to screen for (ant)agonists of (I)/(II) activity, particularly antibacterials. (III), e.g. Ab, are used to treat conditions requiring inhibition of gluS, generally any S. pneumoniae infection but particularly meningitis. Fragments of (I) are useful as probes to isolate full-length or related sequences, or for diagnosis, e.g. by polymerase chain

reaction, of the stage and type of an infection, including detection of mutations and polymorphisms. Diagnosis may also be done by detecting overexpression of the gluS genes, e.g. by immunoassay. Ab are used to treat infections; to isolate/identify (II)-expressing clones; to purify (II) and as immunoassay reagents. More generally, (I)-(III) can prevent adhesion of bacteria to wounds, in-dwelling devices etc.; block gluS-protein mediated invasion of mammalian cells and block normal progression of infection. Treatment of in-dwelling devices with (II) before insertion is also contemplated. Dwg.0/0

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FILE		FFULL' ENTERED AT 15:11:29 ON 31 JUL 2002
L10	602	SEA FILE=HCAPLUS ABB=ON PLU=ON ((STREPTOCOCC? OR
		S) (W) PNEUMON?) (5A) INFECTION
L15 .	176	SEA FILE=HCAPLUS ABB=ON PLU=ON L10(S)(TREAT? OR
		THERAP? OR PROPHYL?)
L16	25	SEA FILE=HCAPLUS ABB=ON PLU=ON L15(S) (PROTEIN OR
		POLYPROTEIN OR PEPTIDE OR POLYPEPTIDE)
L17	206	SEA L16
L23	3	SEA FILE=USPATFULL ABB=ON PLU=ON L17(S)(INHIBIT? OR
		ANTAGON? OR INTERFER?)

L23 ANSWER 1 OF 3 USPATFULL

ACCESSION NUMBER:

2002:164767 USPATFULL

TITLE:

Novel era

INVENTOR(S):

Black, Michael Terence, Chester Springs, PA,

UNITED STATES

Hodgson, John Edward, Malvern, PA, UNITED STATES Knowles, David Justin Charles, Boroughbridge,

UNITED KINGDOM

Lonetto, Michael Arthur, Collegeville, PA, UNITED

STATES

Nicholas, Richard Oakley, Collegeville, PA,

UNITED STATES

Palmer, Leslie Marie, Audubon, PA, UNITED STATES Reid, Robert, East Norriton, PA, UNITED STATES Rosenberg, Martin, Royersford, PA, UNITED STATES Zarfos, Phillip, Norristown, PA, UNITED STATES

	NUMBER	KIND	DATE
US	2002086385	A1	:20020704
US	2001-820407	A1	20010329

APPLICATION INFO.: RELATED APPLN. INFO.:

PATENT INFORMATION:

Division of Ser. No. US 1997-965130, filed on 6

Nov 1997, GRANTED, Pat. No. US 6287803

NUMBER	DATE
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PRIORITY INFORMATION:

US 1996-31879P 19961127 (60)

Utility DOCUMENT TYPE: FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE:

DECHERT, ATTN: ALLEN BLOOM, ESQ, 4000 BELL

ATLANTIC TOWER, 1717 ARCH STREET, PHILADELPHIA,

PA, 19103

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

20

LINE COUNT:

1608

Searcher :

Shears

308-4994

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention provides era polypeptides and DNA (RNA) encoding era AΒ polypeptides and methods for producing such polypeptides by recombinant techniques. Also provided are methods for utilizing era polypeptides to screen for antibacterial compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/183.000

INCLS: 435/069.100; 435/252.300; 435/320.100; 536/023.200

NCL NCLM: 435/183.000

ASSISTANT EXAMINER:

NUMBER OF CLAIMS:

LEGAL REPRESENTATIVE:

435/069.100; 435/252.300; 435/320.100; 536/023.200

L23 ANSWER 2 OF 3 USPATFULL

2002:137146 USPATFULL ACCESSION NUMBER:

Antibodies to neutrokine-alpha TITLE:

INVENTOR(S):

Yu, Guo-Liang, Berkeley, CA, United States

Ebner, Reinhard, Gaithersburg, MD, United States

Ni, Jian, Rockville, MD, United States

Rosen, Craig A., Laytonsville, MD, United States

Human Genome Sciences, Inc., Rockville, MD, PATENT ASSIGNEE(S):

United States (U.S. corporation)

NUMBER KIND US 6403770 20020611 PATENT INFORMATION: В1 20000608 APPLICATION INFO.: US 2000-589287 (9) Continuation of Ser. No. US 2000-507968, filed on RELATED APPLN. INFO .: 22 Feb 2000 Continuation-in-part of Ser. No. US 1999-255794, filed on 23 Feb 1999 Continuation-in-part of Ser. No. US 1998-5874, filed on 12 Jan 1998 Continuation-in-part of Ser. No. WO 1996-US17957, filed on 25 Oct 1996

-	•	110.	"	1000	0,01733	′′	11100	011	20
		•		NUMB	ER		DATE		
PRIORITY	INFORMATION:	US	2000	)-176	015P	20	000114	1 (	60)
		US	1999	9-171	626P	19	991223	3 (	60)
		US	1999	9-171	108P	19	991216	5 (	60)
	•	US	1999	-168	624P	19	991203	3 (	60)
	•	US	1999	9-167	239P	19	991124	1 (	60)
		US	1999	-145	824P	19	990727	7 (	60)
	** 	US	1999	-142	659P	19	990706	5 (	60)
		US	1999	9-136	784P	19	990528	3 (	60)
	•	US	1999	9-131	673P	19	990429	) (	60)
		US	1999	9-131	278P	19	990427	7 (	60)
•		US	1999	-130	696P	19	990423	3 (	60)
	•	US	1999	-130	412P	19	990416	5 (	60)
		US	1999	9-127	598P	19	990402	2 (	60)
		US	1999	9-126	599P	19	990326	5 (	60)
•	•	US	1999	-124	097P	19	990312	2 (	60)
		US	1999	122	388P	19	990302	2 (	60)
		US	1997	7-361	00P	19	970114	1 (	60)
DOCUMENT	TYPE:	Uti	lity	7					
FILE SEGN	MENT:	GRA	ANTEÏ	)					
PRIMARY I	EXAMINER:	Kur	nz, C	Gary	L.				

Prasad, Sarada C

292

Human Genome Sciences, Inc.

308-4994 Searcher : Shears

EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 11 Drawing Figure(s); 22 Drawing Page(s)

15430 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a novel Neutrokine-alpha, and a splice variant thereof designated Neutrokine-alphaSV, polynucleotides and polypeptides which are members of the TNF family. In particular, isolated nucleic acid molecules are provided encoding the human Neutrokine-alpha and/or Neutrokine-alphaSV polypeptides, including soluble forms of the extracellular domain. Neutrokine-alpha and/or Neutrokine-alphaSV polypeptides are also provided as are vectors, host cells and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of Neutrokine-alpha and/or Neutrokine-alphaSV activity. Also provided are diagnostic methods for detecting immune system-related disorders and therapeutic methods for treating immune system-related disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 530/387.300

INCLS: 530/300.000; 530/324.000; 530/388.100; 530/388.230;

530/351.000; 435/069.500; 435/007.100

NCLM: NCL 530/387.300

435/007.100; 435/069.500; 530/300.000; 530/324.000; NCLS:

530/351.000; 530/388.100; 530/388.230

L23 ANSWER 3 OF 3 USPATFULL

ACCESSION NUMBER: 2002:126317 USPATFULL

TITLE: Human tumor necrosis factor delta and epsilon

INVENTOR(S): Yu, Guo-Liang, Berkeley, CA, UNITED STATES

Ni, Jian, Germantown, MD, UNITED STATES

Gentz, Reiner L., Rockville, MD, UNITED STATES Dillon, Patrick J., Carlsbad, CA, UNITED STATES

PATENT ASSIGNEE(S): Human Genome Sciences, Inc., Rockville, MD,

UNITED STATES, 20850 (U.S. corporation)

NUMBER KIND DATE US 2002064829 PATENT INFORMATION: A1 20020530 A1 APPLICATION INFO.: US 2001-879919 20010614 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1997-815783,

filed on 12 Mar 1997, PENDING

NUMBER DATE US 1996-16812P 19960314 (60) PRIORITY INFORMATION: US 2001-293499P 20010525 (60) US 2001-277978P 20010323 (60) US 2001-276248P 20010316 (60) 20001213 (60) US 2000-254875P US 2000-241952P 20001023 (60) 20000615 (60) US 2000-211537P

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE,

ROCKVILLE, MD, 20850

NUMBER OF CLAIMS:

308-4994 Searcher : Shears

EXEMPLARY CLAIM:

1

NUMBER OF DRAWINGS:

11 Drawing Page(s)

LINE COUNT:

13531

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB

L27

The invention relates to human TNF delta and TNF epsilon polypeptides, polynucleotides encoding the polypeptides, methods for producing the polypeptides, in particular by expressing the polynucleotides, and agonists and antagonists of the polypeptides. The invention further relates to methods for utilizing such polynucleotides, polypeptides, agonists and antagonists for applications, which relate, in part, to research, diagnostic and clinical arts.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/069.100

INCLS: 435/325.000; 435/320.100; 530/351.000; 424/145.100;

530/388.230; 536/023.500

NCL NCLM: 435/069.100

NCLS: 435/325.000; 435/320.100; 530/351.000; 424/145.100;

530/388.230; 536/023.500

FILE "ECAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, USPATFULL' ENTERED AT 15:12:52 ON 31 JUL 2002)

L25 2953 S GILBERT C?/AU L26 61 S HANSBRO P?/AU

61 S HANSBRO P?/AU 2 S L25 AND L26

4 S (L25 OR L26) AND L15

4 S L27 OR L28

3 DUP REM 1.29 (1- DUPLICATE REMOVED)

L30 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS

US COPYRIGHT 2002 ACS DUPLICATE 1 2000:98775 HCAPLUS

ACCESSION NUMBER:

DOCUMENT NUMBER: 132:162046

TITLE: Sequences of Streptococcus pneumoniae proteins

and nucleic acid molecules, and uses thereof in in drug screening, diagnostic, and therapeutic

- Author (5)

applications

INVENTOR(S): Gilbert, Christophe François Guy;

Hansbro, Philip Michael

PATENT ASSIGNEE(S): M

Microbial Technics Limited, UK PCT Int. Appl., 108 pp.

SOURCE: PCT Int. Appl CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2000006737 A2 20000210 WO 1999-GB2451 19990727

WO 2000006737 A3 20000629

W: CN, JP, US RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,

NL, PT, SE

ÉP 1100921 A2 20010523 EP 1999-934989 19990727

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,

PT, IE, FI

PRIORITY APPLN. INFO.: GB 1998-16337 A 19980727

US 1999-125164P P 19990319 WO 1999-GB2451 W 19990727

AB The invention provides sequences of novel protein antigens from type 4 Streptococcus pneumoniae. The invention also provides for the use of the disclosed nucleic acids/proteins as antigens/immunogens, in the diagnosis of Streptococcus infections, and in screening for potential antimicrobial agents.

L30 ANSWER 2 OF 3 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

2000-656168 [63] WPIDS

CROSS REFERENCE:

2001-451553 [48]

DOC. NO. NON-CPI:

N2000-486434 C2000-198585

TITLE:

Novel antigens from Streptococcus pneumoniae of

specific molecular weights useful for

treatment, prophylaxis and diagnosis of Streptococcus

pneumoniae infections.

DERWENT CLASS:

B04 D16 S03

INVENTOR(S):

CRIPPS, A W; HANSBRO, P M; JOMAA, M; KYD,

J M; WELLS, J M

PATENT ASSIGNEE(S):

(PROV-N) PROVALIS UK LTD

COUNTRY COUNT:

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2000058475 A2 20001005 (200063)\* EN 45

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: CN JP US

EP 1165795 A2 20020102 (200209) EN

22

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

CN 1345375 A 20020417 (200248)

# APPLICATION DETAILS:

PATENT NO K	IND	API	PLICATION	DATE
WO 2000058475 EP 1165795			2000-GB1167 2000-912834	20000327 20000327
CN 1345375	Δ		LUUU ULLLU.	20000327
CM 12422/2	T .	CIA	2000 00000	20000027

# FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1165795	A2 Based on	WO 200058475

PRIORITY APPLN. INFO: GB 1999-28678 19991203; GB 1999-7114 19990326

AN 2000-656168 [63] WPIDS

CR 2001-451553 [48]

AB WO 200058475 A UPAB: 20020730

NOVELTY - A protein or polypeptide (I) obtained from Streptococcus pneumoniae and having specific molecular weight as determined by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and specific N-terminal sequences, is new.

DETAILED DESCRIPTION - A protein or polypeptide (I) obtained from Streptococcus pneumoniae and having specific molecular weight as determined by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and specific N-terminal sequences, is new. (I) has a molecular weight of 55, 50, 85, 38, 30, 32, 43 or 100 kDa, and has an N-terminal sequence of ValGluProLysAlaLysProAlaAspPr oSerValVal, AsnAspArqLeuValAlaThrGlnSerAlaAspGlyArgAsnGluSerValLeuMe tSerIleGluThr, GluAspThrThrAsnSerArgPheGlySerGlnPheAspLysTyrArgGlnPr oAsnAlaGlnProAspHisSerHisAspAlaValSerAlaAspAsnSerThrAlaHisAsnArgPheG lvTvrGlvPheAlaIleGlvSerLysTvrIleArgTyr, AspLysTyrArgGlnProAsnAlaGluProAspAspHisHisTyrAlaVal, AspAlaValSerAlaAsp or SerGluThrAsnValTyr, AspLysValAspGluLeuSerAlaLysProAspIleLeuLysPro, GluLeuLysGluGluGly(Trp)ValValLys, and GluValHisAla, respectively. Alternatively, (I) has a molecular weight of less than 14 kDa as determined by SDS-PAGE, and an N-terminal sequence of MetLysLeuAsnGluValLysGluPheValLysGluLeuArgAlaGluThr, AlaLysTyrGluIleLeuTyrIleGluArgProAsnIleGluGluPheAlaLys or Ile(Arg)LeuThrArgMet(Glu)GlyGlyLysLysLysPro(Lys)PheTyrTyr, or has a molecular weight of 16, 27.5, 44 or 12-14 kDa which have a N-terminal sequence of ValMetThrAspProIleAlaAspXLeuXArgIle, (ValAla) (LysGlu) LeuValPheAlaArgHisGlyGlu(LeuThr) Glu(AsnLys), IleIleThrAspValTyrAlaArgGluValLeuAspSerArgGlyAsnProThrLeu, and AlaLeuAsnIleGluAsnIleIleAlaGluIleLysIleAlaSer, respectively. (I) is a reduced toxicity variant or fragment of the above mentioned proteins, preferably has a molecular weight of 16 or 57 kDa under reducing conditions and has the following N-terminal sequence of ArgIleIleLysPheValTyrAlaLys.

INDEPENDENT CLAIMS are also included for the following:

(1) a homologue or derivative (II) of (I);

- (2) one or more antigenic fragments (III) of (I) or (II);
- (3) a nucleic acid molecule (IV) comprising or consisting of a DNA sequence encoding for (I) or their RNA equivalents, a sequence which is complementary or substantially identical to the sequence, or a sequence which codes for (II) or (III);
  - (4) a vector (V) comprising (IV);
  - (5) a host cell (VI) comprising (V);
- (6) an immunogenic/antigenic composition (VII) comprising (I),
  (II) or (III);
  - (7) a vaccine composition (VIII) comprising (IV);
- (8) an antibody (IX) raised against and/or binding to (I), (II) or (III);
- (9) a kit for detecting/diagnosing S. pneumoniae infection comprising (I), (III), (III) or (VII);
- (10) a kit for detecting/diagnosing S. pneumoniae infection comprising (IV);
- (11) determining if (I) represents a potential anti-microbial target involves inactivating the protein or polypeptide, and determining if S. pneumoniae is still viable, in vitro or in vivo;
- (12) use of an agent capable of antagonizing, inhibiting or otherwise interfering with the function or expression of (I) in the manufacture of a medicament for use in **treatment** or **prophylaxis** of **S. pneumoniae** infection; and
  - (13) preparation of (I).

ACTIVITY - Antibacterial. Balb/c mice, 6-10 weeks old were immunized with the immunization protein, prepared by emulsifying 2.5 micro g/ micro L protein in a 1:1 ratio with incomplete Freund's

adjuvant on day 0 by Peyer's patches inoculation and boosted by intratracheal administration 14 days later. On day 21, these mice were challenged with live Streptococcus pneumoniae. Blood was collected, the trachea was exposed and the lung were lavaged by insertion and removal of 0.5 mL sterile phosphate buffered saline (PBS). The recovered fluid (BAL) was assessed for bacterial recovery by plating 10 fold serial dilutions onto blood agar for colony forming units (CFU) determination. The lungs were removed following lavage, placed in 2 mL sterile PBS and homogenized. The lung homogenate was assessed by plating 10-fold serial dilutions onto blood agar for CFU determination. Three proteins assessed in immunization and bacterial challenge showed significant degrees of pulmonary clearance from the lungs. These were proteins with molecular masses of 16, 34 and 57 kDa. A fourth protein of significance was the 12-14 kDa protein which is a toxin and potential virulence component of S. pneumoniae.

MECHANISM OF ACTION - Vaccine; gene therapy.

USE - (I), (II), (III), (IV) or (IX) is useful for detection/diagnosis of S. pneumoniae. (I), (II), (III), (IV) or (VII) is useful for vaccinating a subject against S. pneumoniae. The novel polypeptides, its derivatives or homologs and the nucleic acid molecules are useful in treatment or prophylaxis of S. pneumoniae infection. (All claimed).

DESCRIPTION OF DRAWING(S) - The figure shows the flow chart of the protein purification procedure.

Dwg.2/8

L30 ANSWER 3 OF 3 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

2000-195301 [17] WPIDS

DOC. NO. NON-CPI:

N2000-144461

DOC. NO. CPI:

C2000-060591

TITLE:

Streptococcal proteins and polynucleotides useful

for diagnosis, treatment and prophylaxis of

bacterial infections.

DERWENT CLASS:

B04 D16 S03

INVENTOR(S):

HANNIFFY, S B; HANSBRO, P M; LE PAGE, R W.

F; WELLS, J M

PATENT ASSIGNEE(S):

(MICR-N) MICROBIAL TECHNICS LTD

COUNTRY COUNT:

22

PATENT INFORMATION:

PATENT	NO	KIND	DATE	WEEK	LA	PG

WO 2000006738 A2 20000210 (200017)\* EN 76

RW: AT BE CH CY DE DK ES FI'FR GR GR IE IT LU MC NL PT SE

W: CN JP US

EP 1144640 A2 20011017 (200169) EN

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

CN 1318103 A 20011017 (200213)

# APPLICATION DETAILS:

PATENT NO K	IND	API	PLICATION	DATE
WO 2000006738	A2	WO	1999-GB2452	19990727
EP 1144640	A2	ΕP	1999-934990	19990727
		WO	1999-GB2452	19990727

CN 1318103

19990727 CN 1999-810978

FILING DETAILS:

PATENT NO KIND PATENT NO WO 200006738 ------A2 Based on

PRIORITY APPLN. INFO: US 1999-125329P 19990319; GB 1998-16336

2000-195301 [17]

ΑN AB

NOVELTY - Streptococcus pneumoniae protein or polypeptide (I), its WO 200006738 A UPAB: 20000405 homologs or derivatives, with a fully defined sequence amino acids

DETAILED DESCRIPTION - (I) has an amino acid sequence selected (given in the specification), is new.

from 12 sequences given in the specification. INDEPENDENT CLAIMS are also included for the following:

(1) a protein or polypeptide (II), its homologs or derivatives having a defined amino acid sequence selected from 61 sequences

(2) an antigenic and/or immunogenic fragment of (I), (II) or a given in the specification; protein or polypeptide (III) having a sequence selected from 12 sequences of defined amino acids given in the specification;

- (3) a nucleic acid molecule (IV) encoding (I), (II) or (III) having defined DNA sequences given in the specification (or their RNA equivalents, complementary sequences, homologs, derivatives or identical sequences);
  - (4) an immunogenic and/or antigenic composition (V) comprising (II) or (III) or homologs, derivatives and/or fragments;

- (5) a vaccine composition comprising (III); (6) an antibody (VI) capable of binding to (I), (III) or
- (7) determining the anti-microbial activity of (I) (II) and a homolog, derivative or fragment; and (III) by inactivating the protein and determining the viability of S.pneumoniae.

ACTIVITY - Antiinflammatory; antibacterial.

- MECHANISM OF ACTION Vaccine; antagonist. 100 micro g of recombinant pcDNA3.1 (IV) was injected intramuscularly into the tibialis anterior muscle of both legs of mice. A booster dose was given 4 weeks later and control groups received either non-recombinant pcDNA3.1+DNA or no vaccine. After the second immunization, all mice groups were challenged intra-nasally with a lethal doses of Streptococcus pneumoniae serotype 4 (strain NCTC 11886). Mice were monitored for the development of symptoms associated with the onset of S.pneumoniae induced-disease. The groups vaccinated with DNA survived significantly longer than non-vaccinated controls.
  - USE (I) or homologs, derivatives and/or fragments are useful as an immunogen or antigen and (V) is useful as a vaccine and also in a diagnostic assay. (I-V) are useful for detection or diagnosis of S. pneumoniae, by contacting a sample to be tested with them. Agents capable of antagonizing, inhibiting or interfering with the function or expression of the protein or polypeptide (II) are useful in medical compositions in the treatment or

prophylaxis of S.pneumoniae infection (claimed).

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308-4994

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